N-[(Piperazinyl)hetaryl]arylsulfonamide compounds

Description

5 The present invention relates to novel N-[(piperazinyl)hetaryl]arylsulfonamide compounds. The compounds possess valuable therapeutic properties and are suitable, in particular, for treating diseases which respond to modulation of the dopamine D_3 receptor.

Neurons obtain their information by way of G protein-coupled receptors, inter alia. A large
10 number of substances exert their effect by way of these receptors. One of them is dopamine. Confirmed findings exist with regard to the presence of dopamine and its physiological function as a neurotransmitter. Disturbances in the dopaminergic transmitter system result in diseases of the central nervous system which include, for example, schizophrenia, depression and Parkinson's disease. These diseases, and others, are treated with drugs which
15 interact with the dopamine receptors.

Up until 1990, two subtypes of dopamine receptor had been clearly defined pharmacologically, namely the D_1 and D_2 receptors. More recently, a third subtype was found, namely the D_3 receptor which appears to mediate some effects of antipsychotics and antiparkinsonians
20 (J.C. Schwartz et al., The Dopamine D_3 Receptor as a Target for Antipsychotics, in Novel Antipsychotic Drugs, H.Y. Meltzer, Ed. Raven Press, New York 1992, pages 135-144; M. Dooley et al., Drugs and Aging 1998, 12, 495-514, J.N. Joyce, Pharmacology and Therapeutics 2001, 90, pp. 231-59 "The Dopamine D_3 Receptor as a Therapeutic Target for Antipsychotic and Antiparkinsonian Drugs").
25

Since then, the dopamine receptors have been divided into two families. On the one hand, there is the D_2 group, consisting of D_2, D_3 and D_4 receptors, and, on the other hand, the D_1 group, consisting of D_1 and D_5 receptors. Whereas D_1 and D_2 receptors are widely distributed, D_3 receptors appear to be expressed regioselectively. Thus, these receptors are pref-
30 erentially to be found in the limbic system and the projection regions of the mesolimbic dopamine system, especially in the nucleus accumbens, but also in other regions, such as the amygdala. Because of this comparatively regioselective expression, D_3 receptors are regarded as being a target having few side-effects and it is assumed that while a selective D_3 ligand would have the properties of known antipsychotics, it would not have their dopamine
35 D_2 receptor-mediated neurological side-effects (P. Sokoloff et al., Localization and Function of the D_3 Dopamine Receptor, Arzneim. Forsch./Drug Res. 42(1), 224 (1992); P. Sokoloff et al. Molecular Cloning and Characterization of a Novel Dopamine Receptor (D_3) as a Target for Neuroleptics, Nature, 347, 146 (1990)).

40 Compounds having an affinity for the dopamine D_3 receptor have been described in the prior art on various occasions, e.g. in WO 96/02519, WO 96/02520, WO 96/02249, WO 96/02246 and DE 10131543 and WO 99/02503. Some of these compounds possess high affinities for

the dopamine D_3 receptor. They have therefore been proposed as being suitable for treating diseases of the central nervous system. Some of the compounds described in these publications possess a piperazinylhetaryl structure.

5   The invention is based on the object of providing compounds which act as selective dopamine D_3 receptor ligands.

This object is achieved by means of N-[(piperazinyl)hetaryl]arylsulfonamide compounds of the general formula I

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$$R^1-N \overbrace{}^{} N-Q-R-SO_2-Ar \qquad (I)$$
$$(R^2)_n$$
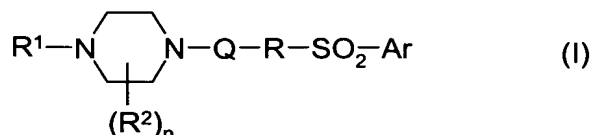
in which

R   is oxygen, a group $N-R^3$ or a group $CR^{3a}R^{3b}$;

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Q   is a bivalent, 6-membered heteroaromatic radical which possesses 1 or 2 N atoms as ring members and which optionally carries one or two substituents R^a which is/are selected, independently of each other, from halogen, CN, NO_2, CO_2R^4, COR^5, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkyl, NH_2, NHR^6, NR^6R^7 and C_1-C_4-

20   haloalkoxy;

Ar   is phenyl or a 6-membered heteroaromatic radical which possesses 1 or 2 N atoms as ring members and which optionally carries one or two substituents R^b, which is/are selected from halogen, NO_2, CN, CO_2R^4, COR^5, NH_2, NHR^6, NR^6R^7,

25   C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, C_3-C_6-cycloalkoxy, C_3-C_6-cycloalkyl-C_1-C_4-alkyl and C_1-C_4-haloalkyl, with it also being possible for two radicals R^b which are bonded to adjacent C atoms of Ar to be together C_3-C_4-alkylene;

30   n   is 0, 1 or 2;

R¹   is hydrogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_3-C_6-cycloalkyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_3-C_4-alkenyl or C_3-C_4-alkynyl;

35   R²   is C_1-C_4-alkyl, C_1-C_4-haloalkyl or, together with R^1, is C_2-C_5-alkylene or, in the case of n = 2, the two radicals R^2 can together be C_1-C_4-alkylene;

2

R^3 is hydrogen or C$_1$-C$_4$-alkyl;

R^{3a}, R^{3b} are, independently of each other, hydrogen or C$_1$-C$_4$-alkyl;

5   R^4 is C$_1$-C$_4$-alkyl, C$_1$-C$_4$-haloalkyl, C$_2$-C$_4$-alkenyl C$_3$-C$_6$-cycloalkyl, C$_3$-C$_6$-cycloalkyl-C$_1$-C$_4$-alkyl, phenyl or benzyl;

R^5 is hydrogen, C$_1$-C$_4$-alkyl, C$_1$-C$_4$-haloalkyl, C$_2$-C$_4$-alkenyl C$_3$-C$_6$-cycloalkyl, C$_3$-C$_6$-cycloalkyl-C$_1$-C$_4$-alkyl, phenyl or benzyl; and

10

R^6, R^7 are each independently selected from C$_1$-C$_4$-alkyl, C$_1$-C$_4$-haloalkyl or together with the nitrogen to which they are bound form a saturated 3-, 4-, 5- or 6-membered heterocycle, which additionally may comprise an oxygen atom or an additional nitrogen atom as a ring member and which may carry 1, 2, 3 or 4 C$_1$-C$_4$ alkyl groups;

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the N-oxides thereof and the physiologically tolerated acid addition salts of these compounds.

These compounds have not previously been described, with the exception of 4-methyl-N-[6-
20   (4-methylpiperazin-1-yl)pyridin-3-yl)benzenesulfonamide and 4-chloro-N-[6-(4-methylpiperazin-1-yl)pyridin-3-yl)benzenesulfonamide, which are offered for sale by Ambinter, Paris, as test substances for exploratory libraries.

The present invention therefore relates to N-[(piperazinyl)hetaryl]arylsulfonamide com-
25   pounds of the general formula I, to their N-oxides and to their physiologically tolerated acid addition salts, with the exception of the compounds 4-methyl-N-[6-(4-methylpiperazin-1-yl)pyridin-3-yl)benzenesulfonamide and 4-chloro-N-[6-(4-methylpiperazin-1-yl)pyridin-3-yl)benzenesulfonamide.

30   The present invention also relates to the use of N-[(piperazinyl)hetaryl]arylsulfonamide compounds of the general formula I, of their N-oxides and of their acid addition salts for producing a pharmaceutical composition for treating diseases which respond to the influence of dopamine-D$_3$ receptor antagonists or agonists.

35   The diseases which respond to the influence of dopamine D$_3$ receptor antagonists or agonists include, in particular, disturbances and diseases of the central nervous system, in particular affective disturbances, neurotic disturbances, stress disturbances and somatoform disturbances and psychoses, especially schizophrenia and depression and, in addition, disturbances of kidney function, in particular kidney function disturbances which are caused by
40   diabetes mellitus (see WO 00/67847)..

According to the invention, at least one compound of the general formula I having the meanings mentioned at the outset is used for treating the abovementioned indications. Provided the compounds of the formula I possess one or more centers of asymmetry, it is also possi-
5   ble to use enantiomeric mixtures, in particular racemates, diastereomeric mixtures and tautomeric mixtures, preferably, however, the respective essentially pure enantiomers, diastereomers and tautomers.

It is likewise possible to use physiologically tolerated salts of the compounds of the formula I,
10   especially acid addition salts with physiologically tolerated acids. Examples of suitable physiologically tolerated organic and inorganic acids are hydrochloric acid, hydrobromic acid, phosphoric acid, sulfuric acid, C_1-C_4-alkylsulfonic acids, such as methanesulfonic acid, aromatic sulfonic acids, such as benzenesulfonic acid and toluenesulfonic acid, oxalic acid, maleic acid, fumaric acid, lactic acid, tartaric acid, adipic acid and benzoic acid. Other utiliz-
15   able acids are described in Fortschritte der Arzneimittelforschung [Advances in drug research], Volume 10, pages 224 ff., Birkhäuser Verlag, Basel and Stuttgart, 1966.

It is likewise possible to use N-oxides of the compounds of the formula I. In the N-oxides of the compounds of the formula I, one or more of the N atoms which is/are ring members, and
20   in particular ring members in the aromatic heterocycles Q and/or Ar, are present as an N-oxide group. Preference is given to those N-oxides of the formula I in which the ring nitrogen atoms in the piperazine ring do not form any N-oxide group. Particularly preferred N-oxides exhibit a N-oxide group on one or two of the ring nitrogen atoms of Ar and/or Q.

25   Here and in that which follows, halogen is fluorine, chlorine, bromine or iodine.

C_n-C_m-Alkyl (in radicals such as alkoxy, alkoxyalkyl, alkylthio, alkylamino, dialkylamino etc., as well) is a straight-chain or branched alkyl group having from n to m carbon atoms, e.g. from 1 to 4 carbon atoms. Examples of an alkyl group are methyl, ethyl, n-propyl, iso-propyl,
30   n-butyl, 2-butyl, iso-butyl, tert-butyl, n-pentyl, 2-pentyl, neopentyl, n-hexyl and the like.

C_1-C_4-Haloalkyl (in radicals such as haloalkoxy, haloalkoxyalkyl, haloalkylthio, etc., as well) is an alkyl group having from 1 to 4 C atoms in which all or some, e.g. 1, 2, 3 or 4 of the hydrogen atoms, is/are replaced by halogen atoms, in particular by chlorine or fluorine. Pre-
35   ferred haloalkyl is C_1-C_2-fluoroalkyl or C_1-C_2-fluorochloroalkyl, in particular CF_3, CHF_2, CF_2Cl, CH_2F, and CH_2CF_3.

C_1-C_4-Hydroxyalkyl is a C_1-C_4-alkyl group which possesses an OH group, such as 2-hydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, 2-hydroxybutyl, 3-hydroxybutyl, 2-methyl-2-
40   hydroxypropyl etc.

C_1-C_4-Alkoxy-C_1-C_4-alkyl is a C_1-C_4-alkyl group which carries a C_1-C_4-alkoxy substituent, e.g. methoxymethyl, ethoxymethyl, 2-methoxyethyl, 1-methoxyethyl, 2-ethoxyethyl, 1-ethoxyethyl, n-propoxymethyl, isopropoxymethyl, n-butoxymethyl, (1-methylpropoxy)methyl,

5   (2-methylpropoxy)methyl, CH_2–$OC(CH_3)_3$, 2-(methoxy)ethyl, 2-(ethoxy)ethyl, 2-(n-propoxy)ethyl, 2-(1-methylethoxy)ethyl, 2-(n-butoxy)ethyl, 2-(1-methylpropoxy)ethyl, 2-(2-methylpropoxy)ethyl, 2-(1,1-dimethylethoxy)ethyl, 2-(methoxy)propyl, 2-(ethoxy)propyl, 2-(n-propoxy)propyl, 2-(1-methylethoxy)propyl, 2-(n-butoxy)propyl, 2-(1-methylpropoxy)propyl, 2-(2-methylpropoxy)propyl, 2-(1,1-dimethylethoxy)propyl, 3-(methoxy)propyl, 3-(ethoxy)propyl,

10   3-(n-propoxy)propyl, 3-(1-methylethoxy)propyl, 3-(n-butoxy)propyl, 3-(1-methylpropoxy)propyl, 3-(2-methylpropoxy)propyl, 3-(1,1-dimethylethoxy)propyl, 2-(methoxy)butyl, 2-(ethoxy)butyl, 2-(n-propoxy)butyl, 2-(1-methylethoxy)butyl, 2-(n-butoxy)butyl, 2-(1-methylpropoxy)butyl, 2-(2-methylpropoxy)butyl, 2-(1,1-dimethylethoxy)butyl, 3-(methoxy)butyl, 3-(ethoxy)butyl, 3-(n-propoxy)butyl, 3-(1-

15   methylethoxy)butyl, 3-(n-butoxy)butyl, 3-(1-methylpropoxy)butyl, 3-(2-methylpropoxy)butyl, 3-(1,1-dimethylethoxy)butyl, 4-(methoxy)butyl, 4-(ethoxy)butyl, 4-(n-propoxy)butyl, 4-(1-methylethoxy)butyl, 4-(n-butoxy)butyl, 4-(1-methylpropoxy)butyl, 4-(2-methylpropoxy)butyl or 4-(1,1-dimethylethoxy)butyl, preferably methoxymethyl, ethoxymethyl, 2-methoxyethyl, 2-ethoxyethyl, 2-(methoxy)propyl, 2-(ethoxy)propyl or 3-(methoxy)propyl, or 3-(ethoxy)propyl.

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C_3-C_6-Cycloalkyl is a cycloaliphatic radical having from 3 to 6 C atoms, such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl.

C_3-C_6-Cycloalkyl-C_1-C_4-alkyl is a C_1-C_4-alkyl group which carries a C_3-C_6-cycloalkyl radical,

25   e.g. cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, 1-cyclopropylethyl, 1-cyclobutylethyl, 1-cyclopentylethyl, 2-cyclopropylethyl, 2-cyclobutylethyl, 2-cyclopentylethyl, 1-cyclopropylpropyl, 1-cyclobutylpropyl, 1-cyclopentylpropyl, 2-cyclopropylpropyl, 2-cyclobutylpropyl, 2-cyclopentylpropyl, 3-cyclopropylpropyl, 3-cyclobutylpropyl, 3-cyclopentylpropyl, 1-cyclopropyl-1-methylethyl, 1-cyclopentyl-1-methylethyl, 1-cyclopentyl-1-

30   methylethyl, 3-cyclohexylpropyl, 1-cyclohexyl-1-methylethyl, 1-cyclohexyl-1-methylethyl or 1-cyclohexyl-1-methylethyl.

C_2-C_4-Alkenyl (in radicals such as alkenyloxy as well) is a singly unsaturated hydrocarbon radical having 2, 3, 4, 5 or 6 C-atoms, e.g. vinyl, allyl(2-propen-1-yl), 1-propen-1-yl, 2-

35   propen-2-yl, methallyl(2-methylprop-2-en-1-yl) and the like. C_3-C_4-Alkenyl is, in particular, allyl, 1-methylprop-2-en-1-yl, 2-buten-1-yl, 3-buten-1-yl, methallyl, 2-penten-1-yl, 3-penten-1-yl, 4-penten-1-yl, 1-methylbut-2-en-1-yl or 2-ethylprop-2-en-1-yl.

C_3-C_6-Alkynyl (in radicals such as alkinyloxy as well) is a hydrocarbon radical having 2, 3, 4, 5 or 6 C atoms which possesses a triple bond, e.g. propargyl (2-propyn-1-yl), 1-methylprop-2-yn-1-yl, 2-butyn-1-yl, 3-butyn-1-yl, 2-pentyn-1-yl, 1-pentyn-3-yl, etc.

5   Examples of 6-membered heteroaromatic radicals which possess 1 or 2 nitrogen atoms as ring members are, in particular, 2-, 3- or 4-pyridinyl, 2-, 4- or 5-pyrimidinyl, 2- or 3-pyrazinyl and 3- or 4-pyridazinyl. Examples of bivalent, 6-membered heteroaromatic radicals which possess 1 or 2 nitrogen atoms as ring members are, in particular, pyridin-2,4-diyl, pyridin-2,5-diyl, pyridin-2,6-diyl, pyridin-3,5-diyl, pyrimidin-2,4-diyl, pyrimidin-2,5-diyl, pyrimidin-4,6-
10   diyl, pyrazin-2,5-diyl, pyrazin-2,6-diyl, pyridazin-3,6-diyl and pyridazin-3,5-diyl.

With regard to using the compounds according to the invention as dopamine D_3 receptor ligands, preference is given to those compounds of formula I in which the piperazin ring is bonded to the heteroaromatic radical Q in the meta position or, in particular, in the para posi-
15   tion with respect to the group R.

In one embodiment the radical R^a is selected from halogen, CN, NO_2, CO_2R^4, COR^5, C_1-C_4-alkyl and C_1-C_4-haloalkyl. Preferred meanings of R^4 and R^5 are, independently of each other, H or C_1-C_4-alkyl. In another embodiement R^a is selected from C_1-C_4-alkoxy, C_1-C_4-
20   haloalkoxy, NH_2, NHR^6 and NR^6R^7. In this embodiment preferred meanings of R^6 and R^7 are independently of each other methyl or ethyl.

The heteroaromatic radical Q may be unsubstituted or possess a substituent R^a which is selected from halogen, C_1-C_4-alkyl and C_1-C_4-haloalkyl, C_1-C_4-alkoxy, NH_2, NHR^6, NR^6R^7
25   and C_1-C_4-haloalkoxy. In one embodiment the radical R^a is selected from halogen, C_1-C_4-alkyl and C_1-C_4-haloalkyl. In another preferred embodiment R^a is selected from C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, NH_2, NHR^6 and NR^6R^7 with specific preference given to methoxy, NH_2, methylamino, dimethylamino, ethylamine, diethylamino and methylethylamino.

30   In a very preferred embodiment, Q is unsubstituted.

In another very preferred embodiment, Q carries a radical selected from C_1-C_4-haloalkoxy, C_1-C_4-alkoxy, C_1-C_4-haloalkyl, C_1-C_4-alkyl, NH_2, NHR^6 or NR^6R^7. and especially methoxy or methyl.
35
Preference is given to the variables Q, R^1, R^2, R^3 and Ar preferably having, independently of each other, the meanings given below:

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Q is preferably a radical of the formula A:

$$\underset{(R^a)_k}{\underset{A_3}{\overset{A_1=A_2}{\diagup}}}\diagup\diagdown$$

(A)
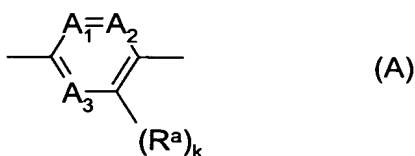
in which A_1, A_2 and A_3 are, independently of each other, N or CH, and one or two of the variables A_1, A_2 and A_3 can also be C-R^a, with A_1, A_2 and A_3 not simultaneously being N or being simultaneously selected from CH and C-R^a. In formula A, k is 0 or 1 and R^a has the previously mentioned meanings.

In formula A, R^a is preferably selected from halogen, especially chlorine or fluorine, C_1-C_4-alkyl, especially methyl, and C_1-C_4-haloalkyl, especially trifluoromethyl, C_1-C_4-alkoxy especially methoxy, C_1-C_4-haloalkoxy, especially difluormethoxy or trifluormethoxy, NH_2, NHR^6 especially methylamino or ethylamino, and NR^6R^7, especially dimethylamino, diethylamino or methylethylamino. The C atom which is located between the atoms A_1 and A_3 preferably carries the piperazinyl radical.

In particular, none of the variables A_1, A_2 and A_3 is C-R^a. Preferred radicals Q are those of formula A, in which A_1 and/or A_3 is/are N, the remaining variable A_1 or A_2 is CH or C-R^a, A_2 is CH, and the piperazinyl radical is bonded to the C atom which is located between A_1 and A_3.

Preference is furthermore given to compounds of the formula I, in which A_1 and A_2 in formula A are N and A_3 is CH or C-R^a.

In a very preferred embodiment k in formula A is 0. In particular, Q is pyridin-2,5-diyl or pyrimidin-2,5-diyl which are unsubstituted or able to possess a substituent R^a which is different from hydrogen. The piperazinyl radical is then preferably arranged in the 2 position.

In another very preferred embodiment k in formula A is 1, A_3 is N, A_1 and A_2 are, independently of each other, N or CH and R^a is selected from C_1-C_4-alkoxy, C_1-C_4-alkyl, NH_2, NHR^6, NR^6R^7 and C_1-C_4-haloalkoxy. In particular R^a is methoxy or methyl. Most preferably the piperazine radical is located in the 2 position. In this embodiment compounds are especially preferred, in which A_1 is N or CH, in particular CH and A_2 is CH.

Ar is preferably phenyl or pyridyl which, where appropriate, possesses one or two of the abovementioned substituents R^b. With regard to using the compounds according to the invention as dopamine D_3 receptor ligands, preference is given to those compounds of formula I in which Ar carries one substituent R^b in the para position and, where appropriate, a further

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substituent R^b in the ortho position or in the metaposition, in each case related to the binding site for the sulfonamide group. The radicals R^b may be identical or different. Preference is given to the radicals R^b in the para position being selected from C_2-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, NH_2, NHR^6 and NR^6R^7.

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In one preferred embodiment the radical R^b in the para position is selected from C_2-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, in particular, from branched C_3-C_6-alkyl, especially isopropyl, and C_3-C_6-cycloalkyl, especially cyclopropyl. Very particular preference is given to the radical R^b which is arranged in the para position of Ar being isopropyl.

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In one preferred embodiment the radical R^b in the para position is selected from NHR^6 and NR^6R^7. In this embodiment preferred meanings of R^6 and R^7 are independently of each other methyl or ethyl or form together with the N atom a saturated 3-, 4-, 5- or 6-membered heterocycle, which additionally may comprise an oxygen atom or an additional nitrogen atom as

15 a ring member and which may carry 1, 2, 3 or 4 C_1-C_4 alkyl groups, e.g. a radical from the group consisting of aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl etc.

Preferred radicals R^b in the meta position or ortho position are selected from halogen, especially chlorine and fluorine, C_1-C_4-alkyl, especially methyl, CN, trifluoromethyl and difluoro-
20 methyl.

With regard to using the compounds according to the invention as dopamine D_3 receptor ligands, preference is given to those compounds of the formula I in which R^1 is different from hydrogen, in particular hydrogen and methyl. In particular, R^1 is C_2-C_3-alkyl, cyclopropyl-
25 methyl or, particularly preferably, ethyl, allyl or n-propyl.

The variable n is preferably 0 or 1. Provided n is $\neq$ 0, R^2 is preferably methyl. When n is $\neq$ 0, the group R^2 is preferably bonded to a carbon atom in the piperazine ring which is adjacent to the group R^1-N. In particularly preferred compounds, n = 0. Particular preference is also
30 given to compounds of the formula I in which it applies that n = 1 and R^2 is a methyl group which is bonded to a carbon atom in the piperazine ring which is adjacent to the group R^1-N. The compounds can then be present as a racemate, as pure enantiomers or as nonracemic mixtures of the enantiomers. Among these, particular preference is given to those compounds in which the C atom which carries the methyl group exhibits the S configuration.

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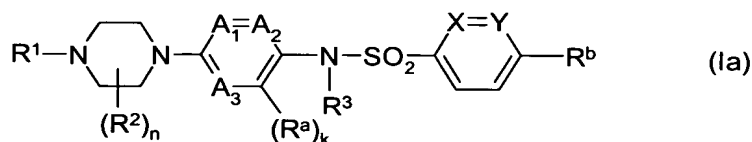R^3 is preferably hydrogen or C_1-C_4-alkyl and, in particular, hydrogen.

If R is a group $CR^{3a}R^{3b}$, at least one of the radicals R^{3a} or R^{3b} is hydrogen. More preferably both radicals R^{3a} and R^{3b} are hydrogen.

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Among the compounds of the general formula I, preference is given to the compounds I, wherein R is N-R^3, wherein R^3 is as defined above and especially H. Amongst these compounds preference is given to the compounds of the general formula Ia

$$R^1-N\overset{\underset{(R^2)_n}{}}{\diagdown}N-\overset{\overset{A_1=A_2}{}}{\underset{\underset{A_3}{}}{}}\overset{}{\diagdown}-\underset{\overset{|}{R^3}}{N}-SO_2-\overset{X=Y}{\diagdown}-R^b \qquad (Ia)$$

in which n, R^1, R^2, R^3, R^a and R^b have the previously mentioned meanings, in particular the meanings specified as being preferred, and in which A_1, A_2 and A_3 are, independently of each other, N or CH, and one of the variables A_1, A_2 and A_3 can also be C-R^a, with A_1, A_2 and A_3 not simultaneously being N or simultaneously being selected from CH and C-R^a, and X and Y are selected from CH, C-$R^{b'}$ and N, in which $R^{b'}$ is halogen, methyl, CN, difluoromethyl or trifluoromethyl, with X and Y not simultaneously being N or simultaneously being C-$R^{b'}$, and k is 0 or 1. R^a has the previously mentioned meanings. In particular, R^a is selected from halogen, especially chlorine or fluorine, C_1-C_4-alkyl, especially methyl, and C_1-C_4-haloalkyl, especially trifluoromethyl, C_1-C_4-alkoxy especially methoxy, C_1-C_4-haloalkoxy, especially difluormethoxy or trifluormethoxy, NH_2, NHR^6 especially methylamino or ethylamino, and NR^6R^7, especially dimethylamino, diethylamino or methylethylamino.

In particular, none of the variables A^1, A^2 and A^3 is C-R^a. Preferred compounds Ia are those in which A_1 and/or A_3 is/are N, the remaining variable A_1 or A_2 is CH or C-R^a, A_2 is CH.

In particular preferred embodiment, k = 0. Among these, preference is furthermore given to compound I in which A_1 and A_2 are N and A_3 is CH or C-R^a. Among these, preference is given to those compounds of the formula Ia in which X or Y is CH or N and, in particular, both are CH.

In another very preferred embodiment k in formula Ia is 1, A_3 is N, A_1 and A_2 are, independently of each other, N or CH and R^a is selected from C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkyl, NH_2, NHR^6, NR^6R^7 and C_1-C_4-haloalkoxy. In particular R^a is methoxy or methyl. In this embodiment compounds are especially preferred, in which A_1 is N or CH, in particular CH and A_2 is CH.

Among the compounds of general formula Ia, preference is given to the compounds of general formula Ia.1

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$$R^1-N\underset{(R^2)_n}{\overset{}{\diagdown}}N-\overset{N=}{\diagdown}\underset{(R^a)_q}{\overset{}{\diagdown}}N-SO_2-\overset{X=Y}{\diagdown}-R^b \qquad (Ia.1)$$

in which n, X, Y, R^1, R^2, R^3, R^a and R^b have the previously mentioned meanings, in particular the meanings specified as being preferred, and q is 0, 1 or 2 and in particular 0 or 1. If q is 1, the radical R^a is preferably bound to the carbon atom which is adjacent to the nitrogen atom
5   of the pyridine ring

Among the compounds of general formula Ia, preference is furthermore given to the compounds of general formula Ia.2

$$R^1-N\underset{(R^2)_n}{\overset{}{\diagdown}}N-\overset{(R^a)_{q'}}{\underset{N\diagdown}{\overset{N=}{\diagdown}}}\underset{(R^a)_q}{\overset{}{\diagdown}}N-SO_2-\overset{X=Y}{\diagdown}-R^b \qquad (Ia.2)$$
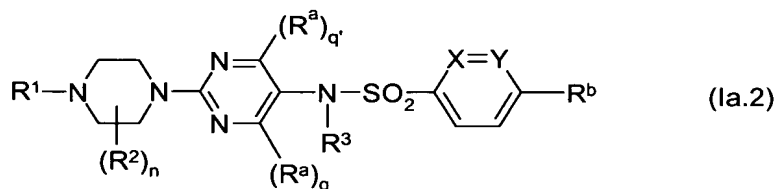
10

in which n, X, Y, R^1, R^2, R^3, R^a and R^b have the previously mentioned meanings, in particular the meanings specified as being preferred, and q and q' are independently of each other 0 or 1, with q+q' preferably being 0 or 1.

15   Examples of compounds of the formula Ia.1 are the compounds of the following general formulae Ia.1a, Ia.1b, Ia.1c, Ia.1d, Ia.1e, Ia.1f, Ia.1g, Ia.1h and Ia.1k:
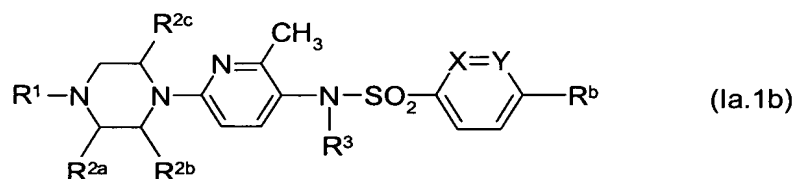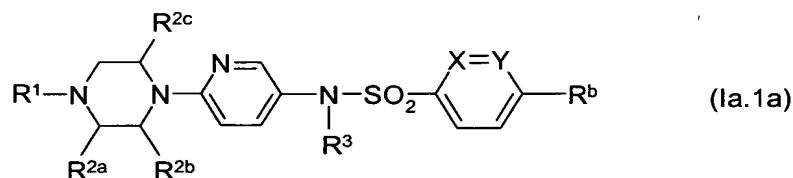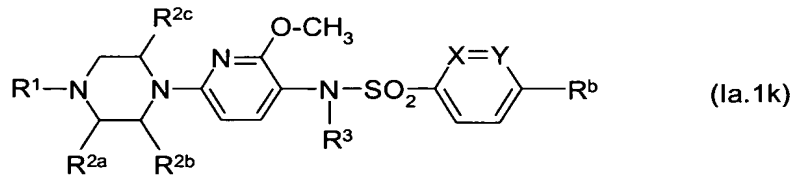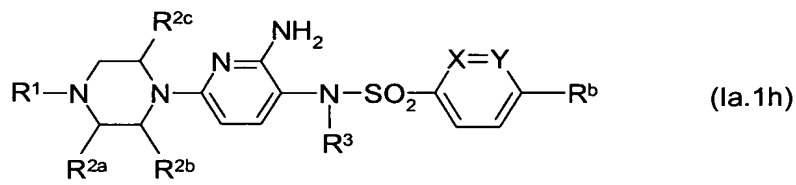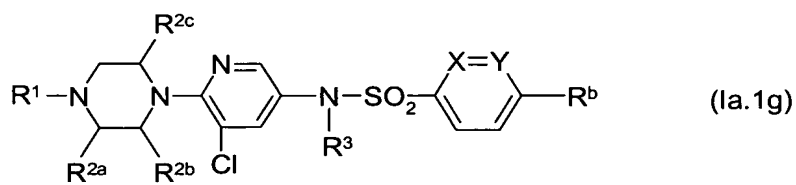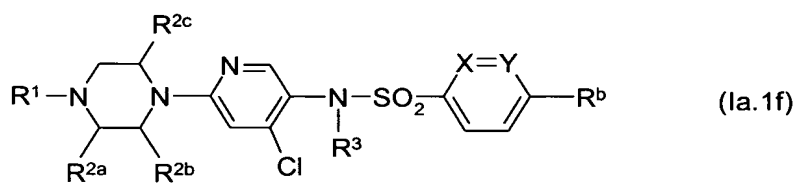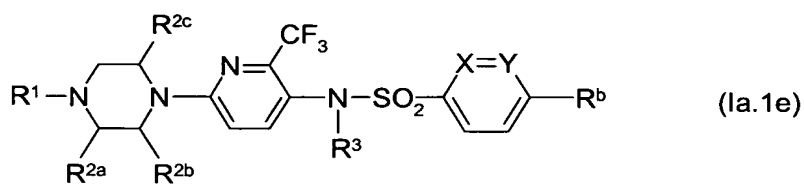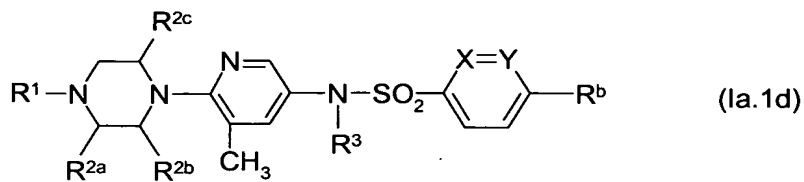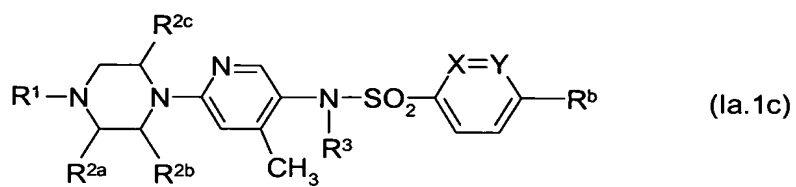
$$R^1-N\underset{R^{2a}\quad R^{2b}}{\overset{R^{2c}}{\diagdown}}N-\overset{N=}{\diagdown}-\underset{R^3}{\overset{}{N}}-SO_2-\overset{X=Y}{\diagdown}-R^b \qquad (Ia.1a)$$

$$R^1-N\underset{R^{2a}\quad R^{2b}}{\overset{R^{2c}}{\diagdown}}N-\overset{N=\ CH_3}{\diagdown}-\underset{R^3}{\overset{}{N}}-SO_2-\overset{X=Y}{\diagdown}-R^b \qquad (Ia.1b)$$

10

(Ia.1c)

(Ia.1d)

(Ia.1e)

(Ia.1f)

5

(Ia.1g)

(Ia.1h)

(Ia.1k)

11

in which R^1, R^{2a}, R^{2b}, R^{2c}, R^3, X, Y and R^b, have the meanings specified in one line in Table 1.

Examples of compounds of the formula Ia.2 are the compounds of the following general formulae Ia.2a, Ia.2b, Ia.2c, Ia.2d and Ia.2e:
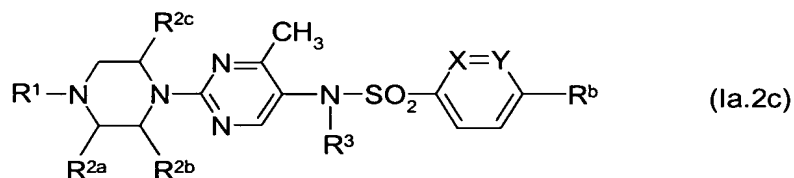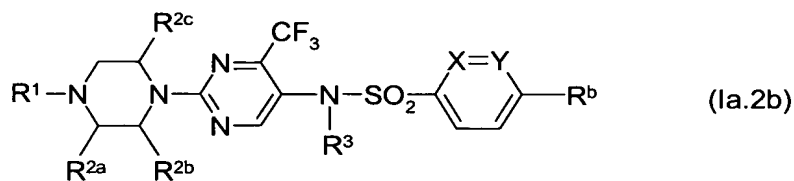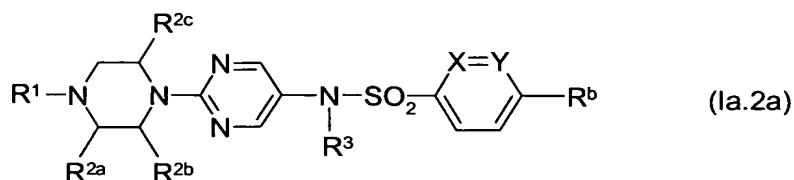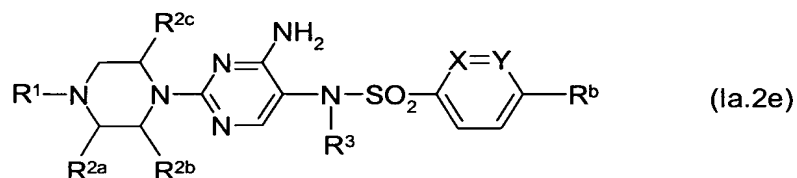
(Ia.2a)

(Ia.2b)

(Ia.2c)

(Ia.2d)

(Ia.2e)

in which R^1, R^{2a}, R^{2b}, R^{2c}, R^3, X, Y and R^b have the meanings specified in one line in Table 1.

Table 1:

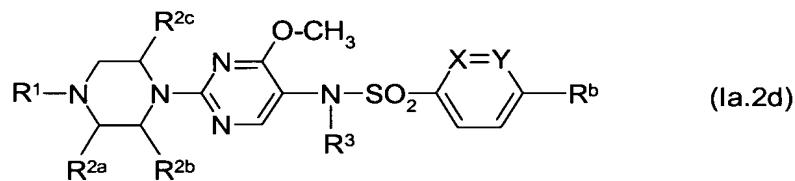| No.	R¹	R²ᵃ	R²ᵇ	R²ᶜ	R³	X	Y	Rᵇ
1.	H	H	H	H	H	CH	CH	CH(CH₃)₂
2.	CH₃	H	H	H	H	CH	CH	CH(CH₃)₂
3.	CH₂CH₃	H	H	H	H	CH	CH	CH(CH₃)₂
4.	CH₂CH=CH₂	H	H	H	H	CH	CH	CH(CH₃)₂
5.	CH₂-c-C₃H₅	H	H	H	H	CH	CH	CH(CH₃)₂
6.	CH₂CH₂CH₃	H	H	H	H	CH	CH	CH(CH₃)₂
7.	H	(s)CH₃	H	H	H	CH	CH	CH(CH₃)₂
8.	CH₃	(s)CH₃	H	H	H	CH	CH	CH(CH₃)₂
9.	CH₂CH₃	(s)CH₃	H	H	H	CH	CH	CH(CH₃)₂
10.	CH₂CH=CH₂	(s)CH₃	H	H	H	CH	CH	CH(CH₃)₂
11.	CH₂-c-C₃H₅	(s)CH₃	H	H	H	CH	CH	CH(CH₃)₂
12.	CH₂CH₂CH₃	(s)CH₃	H	H	H	CH	CH	CH(CH₃)₂
13.	CH₃	*rac*- CH₃	H	H	H	CH	CH	CH(CH₃)₂
14.	CH₂CH=CH₂	*rac*- CH₃	H	H	H	CH	CH	CH(CH₃)₂
15.	CH₂-c-C₃H₅	*rac*- CH₃	H	H	H	CH	CH	CH(CH₃)₂
16.	CH₂CH₂CH₃	*rac*- CH₃	H	H	H	CH	CH	CH(CH₃)₂
17.	CH₃	(R)CH₃	H	H	H	CH	CH	CH(CH₃)₂
18.	CH₂CH=CH₂	(R)CH₃	H	H	H	CH	CH	CH(CH₃)₂
19.	CH₂-c-C₃H₅	(R)CH₃	H	H	H	CH	CH	CH(CH₃)₂
20.	CH₂CH₂CH₃	(R)CH₃	H	H	H	CH	CH	CH(CH₃)₂
21.	CH₃	H	CH₃	H	H	CH	CH	CH(CH₃)₂
22.	CH₂CH=CH₂	H	CH₃	H	H	CH	CH	CH(CH₃)₂
23.	CH₂-c-C₃H₅	H	CH₃	H	H	CH	CH	CH(CH₃)₂
24.	CH₂CH₂CH₃	H	CH₃	H	H	CH	CH	CH(CH₃)₂
25.	CH₃	CH₃	H	CH₃	H	CH	CH	CH(CH₃)₂
26.	CH₂CH=CH₂	CH₃	H	CH₃	H	CH	CH	CH(CH₃)₂
27.	CH₂-c-C₃H₅	CH₃	H	CH₃	H	CH	CH	CH(CH₃)₂
28.	CH₂CH₂CH₃	CH₃	H	CH₃	H	CH	CH	CH(CH₃)₂
29.	CH₃	CH₃	CH₃	H	H	CH	CH	CH(CH₃)₂
30.	CH₂CH=CH₂	CH₃	CH₃	H	H	CH	CH	CH(CH₃)₂
31.	CH₂-c-C₃H₅	CH₃	CH₃	H	H	CH	CH	CH(CH₃)₂
32.	CH₂CH₂CH₃	CH₃	CH₃	H	H	CH	CH	CH(CH₃)₂
33.	(s)(CH₂)₃		H	H	H	CH	CH	CH(CH₃)₂
34.	(s)(CH₂)₄		H	H	H	CH	CH	CH(CH₃)₂
35.	*rac*(CH₂)₃		H	H	H	CH	CH	CH(CH₃)₂
36.	*rac* (CH₂)₄		H	H	H	CH	CH	CH(CH₃)₂
37.	(R)(CH₂)₃		H	H	H	CH	CH	CH(CH₃)₂
38.	(R)(CH₂)₄		H	H	H	CH	CH	CH(CH₃)₂
39.	CH₂CH=CH₂	H	H	H	H	C-Cl	CH	CH(CH₃)₂
40.	CH₂-c-C₃H₅	H	H	H	H	C-Cl	CH	CH(CH₃)₂
41.	CH₂CH₂CH₃	H	H	H	H	C-Cl	CH	CH(CH₃)₂

13

No.	R¹	R²ᵃ	R²ᵇ	R²ᶜ	R³	X	Y	R⁵
42.	$CH_2CH=CH_2$	(s)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
43.	CH_2-c-C_3H_5	(s)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
44.	CH_2CH_3	(s)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
45.	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
46.	$CH_2CH=CH_2$	rac- CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
47.	CH_2-c-C_3H_5	rac- CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
48.	$CH_2CH_2CH_3$	rac- CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
49.	CH_2CH_3	rac- CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
50.	$CH_2CH=CH_2$	(R)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
51.	CH_2-c-C_3H_5	(R)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
52.	CH_2CH_3	(R)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
53.	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
54.	$CH_2CH=CH_2$	H	CH_3	H	H	C-Cl	CH	$CH(CH_3)_2$
55.	CH_2-c-C_3H_5	H	CH_3	H	H	C-Cl	CH	$CH(CH_3)_2$
56.	$CH_2CH_2CH_3$	H	CH_3	H	H	C-Cl	CH	$CH(CH_3)_2$
57.	$CH_2CH=CH_2$	CH_3	H	CH_3	H	C-Cl	CH	$CH(CH_3)_2$
58.	CH_2-c-C_3H_5	CH_3	H	CH_3	H	C-Cl	CH	$CH(CH_3)_2$
59.	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	C-Cl	CH	$CH(CH_3)_2$
60.	$CH_2CH=CH_2$	CH_3	CH_3	H	H	C-Cl	CH	$CH(CH_3)_2$
61.	CH_2-c-C_3H_5	CH_3	CH_3	H	H	C-Cl	CH	$CH(CH_3)_2$
62.	$CH_2CH_2CH_3$	CH_3	CH_3	H	H	C-Cl	CH	$CH(CH_3)_2$
63.	$(CH_2)_3$		H	H	H	C-Cl	CH	$CH(CH_3)_2$
64.	$(CH_2)_4$		H	H	H	C-Cl	CH	$CH(CH_3)_2$
65.	$CH_2CH=CH_2$	H	H	H	H	CH	C-Cl	$CH(CH_3)_2$
66.	CH_2-c-C_3H_5	H	H	H	H	CH	C-Cl	$CH(CH_3)_2$
67.	$CH_2CH_2CH_3$	H	H	H	H	CH	C-Cl	$CH(CH_3)_2$
68.	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
69.	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
70.	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
71.	CH_2CH_3	(s)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
72.	$CH_2CH=CH_2$	rac- CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
73.	CH_2-c-C_3H_5	rac- CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
74.	$CH_2CH_2CH_3$	rac- CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
75.	CH_2CH_3	rac- CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
76.	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
77.	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
78.	CH_2CH_3	(R)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
79.	$CH_2CH_2CH_3$	(R)CH_3	H	H'	H	CH	C-Cl	$CH(CH_3)_2$
80.	$CH_2CH=CH_2$	H	CH_3	H	H	CH	C-Cl	$CH(CH_3)_2$
81.	CH_2-c-C_3H_5	H	CH_3	H	H	CH	C-Cl	$CH(CH_3)_2$
82.	$CH_2CH_2CH_3$	H	CH_3	H	H	CH	C-Cl	$CH(CH_3)_2$

14

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^6
83.	CH$_2$CH=CH$_2$	CH$_3$	H	CH$_3$	H	CH	C-Cl	CH(CH$_3$)$_2$
84.	CH$_2$-c-C$_3$H$_5$	CH$_3$	H	CH$_3$	H	CH	C-Cl	CH(CH$_3$)$_2$
85.	CH$_2$CH$_2$CH$_3$	CH$_3$	H	CH$_3$	H	CH	C-Cl	CH(CH$_3$)$_2$
86.	CH$_2$CH=CH$_2$	CH$_3$	CH$_3$	H	H	CH	C-Cl	CH(CH$_3$)$_2$
87.	CH$_2$-c-C$_3$H$_5$	CH$_3$	CH$_3$	H	H	CH	C-Cl	CH(CH$_3$)$_2$
88.	CH$_2$CH$_2$CH$_3$	CH$_3$	CH$_3$	H	H	CH	C-Cl	CH(CH$_3$)$_2$
89.	(CH$_2$)$_3$		H	H	H	CH	C-Cl	CH(CH$_3$)$_2$
90.	(CH$_2$)$_4$		H	H	H	CH	C-Cl	CH(CH$_3$)$_2$
91.	CH$_2$CH=CH$_2$	H	H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
92.	CH$_2$-c-C$_3$H$_5$	H	H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
93.	CH$_2$CH$_2$CH$_3$	H	H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
94.	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
95.	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
96.	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
97.	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
98.	CH$_2$-c-C$_3$H$_5$	rac- CH$_3$	H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
99.	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
100	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
101	CH$_2$-c-C$_3$H$_5$	(R)CH$_3$	H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
102	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
103	CH$_2$CH=CH$_2$	H	CH$_3$	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
104	CH$_2$-c-C$_3$H$_5$	H	CH$_3$	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
105	CH$_2$CH$_2$CH$_3$	H	CH$_3$	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
106	CH$_2$CH=CH$_2$	CH$_3$	H	CH$_3$	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
107	CH$_2$-c-C$_3$H$_5$	CH$_3$	H	CH$_3$	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
108	CH$_2$CH$_2$CH$_3$	CH$_3$	H	CH$_3$	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
109	CH$_2$CH=CH$_2$	CH$_3$	CH$_3$	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
110	CH$_2$-c-C$_3$H$_5$	CH$_3$	CH$_3$	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
111	CH$_2$CH$_2$CH$_3$	CH$_3$	CH$_3$	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
112	(CH$_2$)$_3$		H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
113	(CH$_2$)$_4$		H	H	H	C-CH$_3$	CH	CH(CH$_3$)$_2$
114	CH$_2$CH=CH$_2$	H	H	H	H	CH	C-CH$_3$	CH(CH$_3$)$_2$
115	CH$_2$-c-C$_3$H$_5$	H	H	H	H	CH	C-CH$_3$	CH(CH$_3$)$_2$
116	CH$_2$CH$_2$CH$_3$	H	H	H	H	CH	C-CH$_3$	CH(CH$_3$)$_2$
117	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	H	CH	C-CH$_3$	CH(CH$_3$)$_2$
118	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	H	CH	C-CH$_3$	CH(CH$_3$)$_2$
119	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	H	CH	C-CH$_3$	CH(CH$_3$)$_2$
120	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	H	CH	C-CH$_3$	CH(CH$_3$)$_2$
121	CH$_2$-c-C$_3$H$_5$	rac- CH$_3$	H	H	H	CH	C-CH$_3$	CH(CH$_3$)$_2$
122	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	H	CH	C-CH$_3$	CH(CH$_3$)$_2$
123	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	H	CH	C-CH$_3$	CH(CH$_3$)$_2$

15

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
124	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
125	$CH_2CH_2CH_3$	(T)CH_3	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
126	$CH_2CH=CH_2$	H	CH_3	H	H	CH	C-CH_3	$CH(CH_3)_2$
127	CH_2-c-C_3H_5	H	CH_3	H	H	CH	C-CH_3	$CH(CH_3)_2$
128	$CH_2CH_2CH_3$	H	CH_3	H	H	CH	C-CH_3	$CH(CH_3)_2$
129	$CH_2CH=CH_2$	CH_3	H	CH_3	H	CH	C-CH_3	$CH(CH_3)_2$
130	CH_2-c-C_3H_5	CH_3	H	CH_3	H	CH	C-CH_3	$CH(CH_3)_2$
131	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	CH	C-CH_3	$CH(CH_3)_2$
132	$CH_2CH=CH_2$	CH_3	CH_3	H	H	CH	C-CH_3	$CH(CH_3)_2$
133	CH_2-c-C_3H_5	CH_3	CH_3	H	H	CH	C-CH_3	$CH(CH_3)_2$
134	$CH_2CH_2CH_3$	CH_3	CH_3	H	H	CH	C-CH_3	$CH(CH_3)_2$
135	$(CH_2)_3$		H	H	H	CH	C-CH_3	$CH(CH_3)_2$
136	$(CH_2)_4$		H	H	H	CH	C-CH_3	$CH(CH_3)_2$
137	H	H	H	H	H	CH	CH	c-C_3H_5
138	CH_3	H	H	H	H	CH	CH	c-C_3H_5
139	CH_2CH_3	H	H	H	H	CH	CH	c-C_3H_5
140	$CH_2CH=CH_2$	H	H	H	H	CH	CH	c-C_3H_5
141	CH_2-c-C_3H_5	H	H	H	H	CH	CH	c-C_3H_5
142	$CH_2CH_2CH_3$	H	H	H	H	CH	CH	c-C_3H_5
143	H	(s)CH_3	H	H	H	CH	CH	c-C_3H_5
144	CH_3	(s)CH_3	H	H	H	CH	CH	c-C_3H_5
145	CH_2CH_3	(s)CH_3	H	H	H	CH	CH	c-C_3H_5
146	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	CH	c-C_3H_5
147	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	CH	c-C_3H_5
148	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	CH	c-C_3H_5
149	CH_3	*rac*-CH_3	H	H	H	CH	CH	c-C_3H_5
150	$CH_2CH=CH_2$	*rac*-CH_3	H	H	H	CH	CH	c-C_3H_5
151	CH_2-c-C_3H_5	*rac*-CH_3	H	H	H	CH	CH	c-C_3H_5
152	$CH_2CH_2CH_3$	*rac*-CH_3	H	H	H	CH	CH	c-C_3H_5
153	CH_2CH_3	(R)CH_3	H	H	H	CH	CH	c-C_3H_5
154	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	CH	c-C_3H_5
155	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	CH	c-C_3H_5
156	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	CH	c-C_3H_5
157	CH_3	H	CH_3	H	H	CH	CH	c-C_3H_5
158	$CH_2CH=CH_2$	H	CH_3	H	H	CH	CH	c-C_3H_5
159	CH_2-c-C_3H_5	H	CH_3	H	H	CH	CH	c-C_3H_5
160	$CH_2CH_2CH_3$	H	CH_3	H	H	CH	CH	c-C_3H_5
161	CH_3	CH_3	H	CH_3	H	CH	CH	c-C_3H_5
162	$CH_2CH=CH_2$	CH_3	H	CH_3	H	CH	CH	c-C_3H_5
163	CH_2-c-C_3H_5	CH_3	H	CH_3	H	CH	CH	c-C_3H_5
164	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	CH	CH	c-C_3H_5

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No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
165	CH$_3$	CH$_3$	CH$_3$	H	H	CH	CH	c-C$_3$H$_5$
166	CH$_2$CH=CH$_2$	CH$_3$	CH$_3$	H	H	CH	CH	c-C$_3$H$_5$
167	CH$_2$-c-C$_3$H$_5$	CH$_3$	CH$_3$	H	H	CH	CH	c-C$_3$H$_5$
168	CH$_2$CH$_2$CH$_3$	CH$_3$	CH$_3$	H	H	CH	CH	c-C$_3$H$_5$
169	(s)(CH$_2$)$_3$		H	H	H	CH	CH	c-C$_3$H$_5$
170	(s)(CH$_2$)$_4$		H	H	H	CH	CH	c-C$_3$H$_5$
171	rac(CH$_2$)$_3$		H	H	H	CH	CH	c-C$_3$H$_5$
172	rac(CH$_2$)$_4$		H	H	H	CH	CH	c-C$_3$H$_5$
173	(R)(CH$_2$)$_3$		H	H	H	CH	CH	c-C$_3$H$_5$
174	(R)(CH$_2$)$_4$		H	H	H	CH	CH	c-C$_3$H$_5$
175	CH$_2$CH=CH$_2$	H	H	H	H	CH	C-Cl	c-C$_3$H$_5$
176	CH$_2$-c-C$_3$H$_5$	H	H	H	H	CH	C-Cl	c-C$_3$H$_5$
177	CH$_2$CH$_2$CH$_3$	H	H	H	H	CH	C-Cl	c-C$_3$H$_5$
178	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	H	CH	C-Cl	c-C$_3$H$_5$
179	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	H	CH	C-Cl	c-C$_3$H$_5$
180	CH$_2$CH$_3$	(s)CH$_3$	H	H	H	CH	C-Cl	c-C$_3$H$_5$
181	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	H	CH	C-Cl	c-C$_3$H$_5$
182	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	H	CH	C-Cl	c-C$_3$H$_5$
183	CH$_2$-c-C$_3$H$_5$	rac- CH$_3$	H	H	H	CH	C-Cl	c-C$_3$H$_5$
184	CH$_2$CH$_3$	rac- CH$_3$	H	H	H	CH	C-Cl	c-C$_3$H$_5$
185	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	H	CH	C-Cl	c-C$_3$H$_5$
186	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	H	CH	C-Cl	c-C$_3$H$_5$
187	CH$_2$-c-C$_3$H$_5$	(R)CH$_3$	H	H	H	CH	C-Cl	c-C$_3$H$_5$
188	CH$_2$CH$_3$	(R)CH$_3$	H	H	H	CH	C-Cl	c-C$_3$H$_5$
189	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	H	CH	C-Cl	c-C$_3$H$_5$
190	CH$_2$CH=CH$_2$	H	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
191	CH$_2$-c-C$_3$H$_5$	H	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
192	CH$_2$CH$_2$CH$_3$	H	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
193	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
194	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
195	CH$_2$CH$_3$	(s)CH$_3$	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
196	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
197	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
198	CH$_2$-c-C$_3$H$_5$	rac- CH$_3$	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
199	CH$_2$CH$_3$	rac- CH$_3$	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
200	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
201	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
202	CH$_2$-c-C$_3$H$_5$	(R)CH$_3$	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
203	CH$_2$CH$_3$	(R)CH$_3$	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
204	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	H	CH	C-CH$_3$	c-C$_3$H$_5$
205	CH$_2$CH=CH$_2$	H	H	H	H	C-Cl	CH	c-C$_3$H$_5$

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No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
206	CH_2-c-C_3H_5	H	H	H	H	C-Cl	CH	c-C_3H_5
207	$CH_2CH_2CH_3$	H	H	H	H	C-Cl	CH	c-C_3H_5
208	$CH_2CH=CH_2$	(s)CH_3	H	H	H	C-Cl	CH	c-C_3H_5
209	CH_2-c-C_3H_5	(s)CH_3	H	H	H	C-Cl	CH	c-C_3H_5
210	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	C-Cl	CH	c-C_3H_5
211	$CH_2CH=CH_2$	rac- CH_3	H	H	H	C-Cl	CH	c-C_3H_5
212	CH_2-c-C_3H_5	rac- CH_3	H	H	H	C-Cl	CH	c-C_3H_5
213	$CH_2CH_2CH_3$	rac- CH_3	H	H	H	C-Cl	CH	c-C_3H_5
214	$CH_2CH=CH_2$	H	H	H	H	C-CH_3	CH	c-C_3H_5
215	CH_2-c-C_3H_5	H	H	H	H	C-CH_3	CH	c-C_3H_5
216	$CH_2CH_2CH_3$	H	H	H	H	C-CH_3	CH	c-C_3H_5
217	$CH_2CH=CH_2$	(s)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
218	CH_2-c-C_3H_5	(s)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
219	CH_2CH_3	(s)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
220	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
221	$CH_2CH=CH_2$	rac- CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
222	CH_2-c-C_3H_5	rac- CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
223	$CH_2CH_2CH_3$	rac- CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
224	$CH_2CH=CH_2$	(R)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
225	CH_2-c-C_3H_5	(R)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
226	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
227	H	H	H	H	H	CH	CH	C_2H_5
228	CH_3	H	H	H	H	CH	CH	C_2H_5
229	CH_2CH_3	H	H	H	H	CH	CH	C_2H_5
230	$CH_2CH=CH_2$	H	H	H	H	CH	CH	C_2H_5
231	CH_2-c-C_3H_5	H	H	H	H	CH	CH	C_2H_5
232	$CH_2CH_2CH_3$	H	H	H	H	CH	CH	C_2H_5
233	H	(s)CH_3	H	H	H	CH	CH	C_2H_5
234	CH_3	(s)CH_3	H	H	H	CH	CH	C_2H_5
235	CH_2CH_3	(s)CH_3	H	H	H	CH	CH	C_2H_5
236	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	CH	C_2H_5
237	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	CH	C_2H_5
238	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	CH	C_2H_5
239	CH_3	rac- CH_3	H	H	H	CH	CH	C_2H_5
240	$CH_2CH=CH_2$	rac- CH_3	H	H	H	CH	CH	C_2H_5
241	CH_2-c-C_3H_5	rac- CH_3	H	H	H	CH	CH	C_2H_5
242	$CH_2CH_2CH_3$	rac- CH_3	H	H	H	CH	CH	C_2H_5
243	CH_3	(R)CH_3	H	H	H	CH	CH	C_2H_5
244	CH_2CH_3	(R)CH_3	H	H	H	CH	CH	C_2H_5
245	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	CH	C_2H_5
246	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	CH	C_2H_5

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^5
247	$CH_2CH_2CH_3$	$(R)CH_3$	H	H	H	CH	CH	C_2H_5
248	CH_3	H	CH_3	H	H	CH	CH	C_2H_5
249	$CH_2CH=CH_2$	H	CH_3	H	H	CH	CH	C_2H_5
250	CH_2-c-C_3H_5	H	CH_3	H	H	CH	CH	C_2H_5
251	$CH_2CH_2CH_3$	H	CH_3	H	H	CH	CH	C_2H_5
252	CH_3	CH_3	H	CH_3	H	CH	CH	C_2H_5
253	$CH_2CH=CH_2$	CH_3	H	CH_3	H	CH	CH	C_2H_5
254	CH_2-c-C_3H_5	CH_3	H	CH_3	H	CH	CH	C_2H_5
255	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	CH	CH	C_2H_5
256	CH_3	CH_3	CH_3	H	H	CH	CH	C_2H_5
257	$CH_2CH=CH_2$	CH_3	CH_3	H	H	CH	CH	C_2H_5
258	CH_2-c-C_3H_5	CH_3	CH_3	H	H	CH	CH	C_2H_5
259	$CH_2CH_2CH_3$	CH_3	CH_3	H	H	CH	CH	C_2H_5
260	$(s)(CH_2)_3$		H	H	H	CH	CH	C_2H_5
261	$(s)(CH_2)_4$		H	H	H	CH	CH	C_2H_5
262	$rac(CH_2)_3$		H	H	H	CH	CH	C_2H_5
263	$rac(CH_2)_4$		H	H	H	CH	CH	C_2H_5
264	$(R)(CH_2)_3$		H	H	H	CH	CH	C_2H_5
265	$(R)(CH_2)_4$		H	H	H	CH	CH	C_2H_5
266	H	H	H	H	H	CH	CH	CH_3
267	CH_3	H	H	H	H	CH	CH	CH_3
268	CH_2CH_3	H	H	H	H	CH	CH	CH_3
269	$CH_2CH=CH_2$	H	H	H	H	CH	CH	CH_3
270	CH_2-c-C_3H_5	H	H	H	H	CH	CH	CH_3
271	$CH_2CH_2CH_3$	H	H	H	H	CH	CH	CH_3
272	H	$(s)CH_3$	H	H	H	CH	CH	CH_3
273	CH_3	$(s)CH_3$	H	H	H	CH	CH	CH_3
274	CH_2CH_3	$(s)CH_3$	H	H	H	CH	CH	CH_3
275	$CH_2CH=CH_2$	$(s)CH_3$	H	H	H	CH	CH	CH_3
276	CH_2-c-C_3H_5	$(s)CH_3$	H	H	H	CH	CH	CH_3
277	$CH_2CH_2CH_3$	$(s)CH_3$	H	H	H	CH	CH	CH_3
278	$CH_2CH=CH_2$	rac-CH_3	H	H	H	CH	CH	CH_3
279	$CH_2CH_2CH_3$	rac-CH_3	H	H	H	CH	CH	CH_3
280	CH_2CH_3	$(R)CH_3$	H	H	H	CH	CH	CH_3
281	$CH_2CH=CH_2$	$(R)CH_3$	H	H	H	CH	CH	CH_3
282	CH_2-c-C_3H_5	$(R)CH_3$	H	H	H	CH	CH	CH_3
283	$CH_2CH_2CH_3$	$(R)CH_3$	H	H	H	CH	CH	CH_3
284	$CH_2CH=CH_2$	H	CH_3	H	H	CH	CH	CH_3
285	$CH_2CH_2CH_3$	H	CH_3	H	H	CH	CH	CH_3
286	$CH_2CH=CH_2$	CH_3	H	CH_3	H	CH	CH	CH_3
287	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	CH	CH	CH_3

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No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
288	CH$_2$CH=CH$_2$	CH$_3$	CH$_3$	H	H	CH	CH	CH$_3$
289	CH$_2$CH$_2$CH$_3$	CH$_3$	CH$_3$	H	H	CH	CH	CH$_3$
290	(s)(CH$_2$)$_3$		H	H	H	CH	CH	CH$_3$
291	(s)(CH$_2$)$_4$		H	H	H	CH	CH	CH$_3$
292	rac(CH$_2$)$_3$		H	H	H	CH	CH	CH$_3$
293	rac(CH$_2$)$_4$		H	H	H	CH	CH	CH$_3$
294	(R)(CH$_2$)$_3$		H	H	H	CH	CH	CH$_3$
295	(R)(CH$_2$)$_4$		H	H	H	CH	CH	CH$_3$
296	H	H	H	H	H	N	CH	CH(CH$_3$)$_2$
297	CH$_3$	H	H	H	H	N	CH	CH(CH$_3$)$_2$
298	CH$_2$CH$_3$	H	H	H	H	N	CH	CH(CH$_3$)$_2$
299	CH$_2$CH=CH$_2$	H	H	H	H	N	CH	CH(CH$_3$)$_2$
300	CH$_2$-c-C$_3$H$_5$	H	H	H	H	N	CH	CH(CH$_3$)$_2$
301	CH$_2$CH$_2$CH$_3$	H	H	H	H	N	CH	CH(CH$_3$)$_2$
302	H	(s)CH$_3$	H	H	H	N	CH	CH(CH$_3$)$_2$
303	CH$_3$	(s)CH$_3$	H	H	H	N	CH	CH(CH$_3$)$_2$
304	CH$_2$CH$_3$	(s)CH$_3$	H	H	H	N	CH	CH(CH$_3$)$_2$
305	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	H	N	CH	CH(CH$_3$)$_2$
306	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	H	N	CH	CH(CH$_3$)$_2$
307	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	H	N	CH	CH(CH$_3$)$_2$
308	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	H	N	CH	CH(CH$_3$)$_2$
309	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	H	N	CH	CH(CH$_3$)$_2$
310	CH$_2$CH$_3$	(R)CH$_3$	H	H	H	N	CH	CH(CH$_3$)$_2$
311	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	H	N	CH	CH(CH$_3$)$_2$
312	CH$_2$-c-C$_3$H$_5$	(R)CH$_3$	H	H	H	N	CH	CH(CH$_3$)$_2$
313	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	H	N	CH	CH(CH$_3$)$_2$
314	(s)(CH$_2$)$_3$		H	H	H	N	CH	CH(CH$_3$)$_2$
315	(s)(CH$_2$)$_4$		H	H	H	N	CH	CH(CH$_3$)$_2$
316	rac(CH$_2$)$_3$		H	H	H	N	CH	CH(CH$_3$)$_2$
317	rac(CH$_2$)$_4$		H	H	H	N	CH	CH(CH$_3$)$_2$
318	(R)(CH$_2$)$_3$		H	H	H	N	CH	CH(CH$_3$)$_2$
319	(R)(CH$_2$)$_4$		H	H	H	N	CH	CH(CH$_3$)$_2$
320	H	H	H	H	H	N	CH	CH=CH$_2$
321	CH$_3$	H	H	H	H	N	CH	CH=CH$_2$
322	CH$_2$CH$_3$	H	H	H	H	N	CH	CH=CH$_2$
323	CH$_2$CH=CH$_2$	H	H	H	H	N	CH	CH=CH$_2$
324	CH$_2$-c-C$_3$H$_5$	H	H	H	H	N	CH	CH=CH$_2$
325	CH$_2$CH$_2$CH$_3$	H	H	H	H	N	CH	CH=CH$_2$
326	H	(s)CH$_3$	H	H	H	N	CH	CH=CH$_2$
327	CH$_3$	(s)CH$_3$	H	H	H	N	CH	CH=CH$_2$
328	CH$_2$CH$_3$	(s)CH$_3$	H	H	H	N	CH	CH=CH$_2$

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No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^5
329	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	H	N	CH	CH=CH$_2$
330	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	H	N	CH	CH=CH$_2$
331	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	H	N	CH	CH=CH$_2$
332	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	H	N	CH	CH=CH$_2$
333	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	H	N	CH	CH=CH$_2$
334	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	H	N	CH	CH=CH$_2$
335	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	H	N	CH	CH=CH$_2$
336	H	H	H	H	H	N	CH	c-C$_3$H$_5$
337	CH$_3$	H	H	H	H	N	CH	c-C$_3$H$_5$
338	CH$_2$CH$_3$	H	H	H	H	N	CH	c-C$_3$H$_5$
339	CH$_2$CH=CH$_2$	H	H	H	H	N	CH	c-C$_3$H$_5$
340	CH$_2$-c-C$_3$H$_5$	H	H	H	H	N	CH	c-C$_3$H$_5$
341	CH$_2$CH$_2$CH$_3$	H	H	H	H	N	CH	c-C$_3$H$_5$
342	H	(s)CH$_3$	H	H	H	N	CH	c-C$_3$H$_5$
343	CH$_3$	(s)CH$_3$	H	H	H	N	CH	c-C$_3$H$_5$
344	CH$_2$CH$_3$	(s)CH$_3$	H	H	H	N	CH	c-C$_3$H$_5$
345	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	H	N	CH	c-C$_3$H$_5$
346	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	H	N	CH	c-C$_3$H$_5$
347	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	H	N	CH	c-C$_3$H$_5$
348	CH$_2$CH$_3$	(R)CH$_3$	H	H	H	N	CH	c-C$_3$H$_5$
349	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	H	N	CH	c-C$_3$H$_5$
350	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	H	N	CH	c-C$_3$H$_5$
351	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	H	N	CH	c-C$_3$H$_5$
352	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	H	N	CH	c-C$_3$H$_5$
353	H	H	H	H	H	N	CH	CH$_3$
354	CH$_3$	H	H	H	H	N	CH	CH$_3$
355	CH$_2$CH$_3$	H	H	H	H	N	CH	CH$_3$
356	CH$_2$CH=CH$_2$	H	H	H	H	N	CH	CH$_3$
357	CH$_2$-c-C$_3$H$_5$	H	H	H	H	N	CH	CH$_3$
358	CH$_2$CH$_2$CH$_3$	H	H	H	H	N	CH	CH$_3$
359	H	(s)CH$_3$	H	H	H	N	CH	CH$_3$
360	CH$_3$	(s)CH$_3$	H	H	H	N	CH	CH$_3$
361	CH$_2$CH$_3$	(s)CH$_3$	H	H	H	N	CH	CH$_3$
362	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	H	N	CH	CH$_3$
363	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	H	N	CH	CH$_3$
364	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	H	N	CH	CH$_3$
365	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	H	N	CH	CH$_3$
366	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	H	N	CH	CH$_3$
367	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	H	N	CH	CH$_3$
368	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	H	N	CH	CH$_3$
369	H	H	H	H	H	N	CH	CF$_3$

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No.	R¹	R²ᵃ	R²ᵇ	R²ᶜ	R³	X	Y	R⁵
370	CH_3	H	H	H	H	N	CH	CF_3
371	CH_2CH_3	H	H	H	H	N	CH	CF_3
372	$CH_2CH=CH_2$	H	H	H	H	N	CH	CF_3
373	CH_2-c-C_3H_5	H	H	H	H	N	CH	CF_3
374	$CH_2CH_2CH_3$	H	H	H	H	N	CH	CF_3
375	H	(s)CH_3	H	H	H	N	CH	CF_3
376	CH_3	(s)CH_3	H	H	H	N	CH	CF_3
377	CH_2CH_3	(s)CH_3	H	H	H	N	CH	CF_3
378	$CH_2CH=CH_2$	(s)CH_3	H	H	H	N	CH	CF_3
379	CH_2-c-C_3H_5	(s)CH_3	H	H	H	N	CH	CF_3
380	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	N	CH	CF_3
381	$CH_2CH=CH_2$	(R)CH_3	H	H	H	N	CH	CF_3
382	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	N	CH	CF_3
383	$CH_2CH=CH_2$	rac- CH_3	H	H	H	N	CH	CF_3
384	$CH_2CH_2CH_3$	rac- CH_3	H	H	H	N	CH	CF_3
385	H	H	H	H	H	CH	N	$CH(CH_3)_2$
386	CH_3	H	H	H	H	CH	N	$CH(CH_3)_2$
387	CH_2CH_3	H	H	H	H	CH	N	$CH(CH_3)_2$
388	$CH_2CH=CH_2$	H	H	H	H	CH	N	$CH(CH_3)_2$
389	CH_2-c-C_3H_5	H	H	H	H	CH	N	$CH(CH_3)_2$
390	$CH_2CH_2CH_3$	H	H	H	H	CH	N	$CH(CH_3)_2$
391	H	(s)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
392	CH_3	(s)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
393	CH_2CH_3	(s)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
394	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
395	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
396	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
397	$CH_2CH=CH_2$	rac- CH_3	H	H	H	CH	N	$CH(CH_3)_2$
398	$CH_2CH_2CH_3$	rac- CH_3	H	H	H	CH	N	$CH(CH_3)_2$
399	CH_2CH_3	(R)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
400	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
401	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
402	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
403	H	H	H	H	H	CH	N	$CH=CH_2$
404	CH_3	H	H	H	H	CH	N	$CH=CH_2$
405	CH_2CH_3	H	H	H	H	CH	N	$CH=CH_2$
406	$CH_2CH=CH_2$	H	H	H	H	CH	N	$CH=CH_2$
407	CH_2-c-C_3H_5	H	H	H	H	CH	N	$CH=CH_2$
408	$CH_2CH_2CH_3$	H	H	H	H	CH	N	$CH=CH_2$
409	H	(s)CH_3	H	H	H	CH	N	$CH=CH_2$
410	CH_3	(s)CH_3	H	H	H	CH	N	$CH=CH_2$

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No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^6
411	CH_2CH_3	(s)CH_3	H	H	H	CH	N	$CH=CH_2$
412	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	N	$CH=CH_2$
413	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	N	$CH=CH_2$
414	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	N	$CH=CH_2$
415	$CH_2CH=CH_2$	rac- CH_3	H	H	H	CH	N	$CH=CH_2$
416	$CH_2CH_2CH_3$	rac- CH_3	H	H	H	CH	N	$CH=CH_2$
417	CH_2CH_3	(R)CH_3	H	H	H	CH	N	$CH=CH_2$
418	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	N	$CH=CH_2$
419	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	N	$CH=CH_2$
420	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	N	$CH=CH_2$
421	H	H	H	H	H	CH	N	c-C_3H_5
422	CH_3	H	H	H	H	CH	N	c-C_3H_5
423	CH_2CH_3	H	H	H	H	CH	N	c-C_3H_5
424	$CH_2CH=CH_2$	H	H	H	H	CH	N	c-C_3H_5
425	CH_2-c-C_3H_5	H	H	H	H	CH	N	c-C_3H_5
426	$CH_2CH_2CH_3$	H	H	H	H	CH	N	c-C_3H_5
427	H	(s)CH_3	H	H	H	CH	N	c-C_3H_5
428	CH_3	(s)CH_3	H	H	H	CH	N	c-C_3H_5
429	CH_2CH_3	(s)CH_3	H	H	H	CH	N	c-C_3H_5
430	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	N	c-C_3H_5
431	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	N	c-C_3H_5
432	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	N	c-C_3H_5
433	$CH_2CH=CH_2$	rac- CH_3	H	H	H	CH	N	c-C_3H_5
434	$CH_2CH_2CH_3$	rac- CH_3	H	H	H	CH	N	c-C_3H_5
435	CH_2CH_3	(R)CH_3	H	H	H	CH	N	c-C_3H_5
436	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	N	c-C_3H_5
437	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	N	c-C_3H_5
438	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	N	c-C_3H_5
439	H	H	H	H	H	CH	N	CH_3
440	CH_3	H	H	H	H	CH	N	CH_3
441	CH_2CH_3	H	H	H	H	CH	N	CH_3
442	$CH_2CH=CH_2$	H	H	H	H	CH	N	CH_3
443	CH_2-c-C_3H_5	H	H	H	H	CH	N	CH_3
444	$CH_2CH_2CH_3$	H	H	H	H	CH	N	CH_3
445	H	(s)CH_3	H	H	H	CH	N	CH_3
446	CH_3	(s)CH_3	H	H	H	CH	N	CH_3
447	CH_2CH_3	(s)CH_3	H	H	H	CH	N	CH_3
448	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	N	CH_3
449	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	N	CH_3
450	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	N	CH_3
451	$CH_2CH=CH_2$	rac- CH_3	H	H	H	CH	N	CH_3

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^6
452	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	H	CH	N	CH$_3$
453	CH$_2$CH$_3$	(R)CH$_3$	H	H	H	CH	N	CH$_3$
454	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	H	CH	N	CH$_3$
455	CH$_2$-c-C$_3$H$_5$	(R)CH$_3$	H	H	H	CH	N	CH$_3$
456	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	H	CH	N	CH$_3$
457	H	H	H	H	H	CH	N	CF$_3$
458	CH$_3$	H	H	H	H	CH	N	CF$_3$
459	CH$_2$CH$_3$	H	H	H	H	CH	N	CF$_3$
460	CH$_2$CH=CH$_2$	H	H	H	H	CH	N	CF$_3$
461	CH$_2$-c-C$_3$H$_5$	H	H	H	H	CH	N	CF$_3$
462	CH$_2$CH$_2$CH$_3$	H	H	H	H	CH	N	CF$_3$
463	H	(s)CH$_3$	H	H	H	CH	N	CF$_3$
464	CH$_3$	(s)CH$_3$	H	H	H	CH	N	CF$_3$
465	CH$_2$CH$_3$	(s)CH$_3$	H	H	H	CH	N	CF$_3$
466	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	H	CH	N	CF$_3$
467	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	H	CH	N	CF$_3$
468	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	H	CH	N	CF$_3$
469	CH$_2$CH$_3$	(R)CH$_3$	H	H	H	CH	N	CF$_3$
470	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	H	CH	N	CF$_3$
471	CH$_2$-c-C$_3$H$_5$	(R)CH$_3$	H	H	H	CH	N	CF$_3$
472	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	H	CH	N	CF$_3$
473	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	H	CH	N	CF$_3$
474	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	H	CH	N	CF$_3$
475	H	H	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
476	CH$_3$	H	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
477	CH$_2$CH$_3$	H	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
478	CH$_2$CH=CH$_2$	H	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
479	CH$_2$-c-C$_3$H$_5$	H	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
480	CH$_2$CH$_2$CH$_3$	H	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
481	H	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
482	CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
483	CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
484	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
485	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
486	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
487	CH$_3$	rac- CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
488	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
489	CH$_2$-c-C$_3$H$_5$	rac- CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
490	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
491	CH$_3$	(R)CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
492	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
493	CH$_2$-c-C$_3$H$_5$	(R)CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
494	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
495	CH$_3$	H	CH$_3$	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
496	CH$_2$CH=CH$_2$	H	CH$_3$	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
497	CH$_2$-c-C$_3$H$_5$	H	CH$_3$	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
498	CH$_2$CH$_2$CH$_3$	H	CH$_3$	H	CH$_3$	CH·	CH	CH(CH$_3$)$_2$
499	CH$_3$	CH$_3$	H	CH$_3$	CH$_3$	CH	CH	CH(CH$_3$)$_2$
500	CH$_2$CH=CH$_2$	CH$_3$	H	CH$_3$	CH$_3$	CH	CH	CH(CH$_3$)$_2$
501	CH$_2$-c-C$_3$H$_5$	CH$_3$	H	CH$_3$	CH$_3$	CH	CH	CH(CH$_3$)$_2$
502	CH$_2$CH$_2$CH$_3$	CH$_3$	H	CH$_3$	CH$_3$	CH	CH	CH(CH$_3$)$_2$
503	CH$_3$	CH$_3$	CH$_3$	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
504	CH$_2$CH=CH$_2$	CH$_3$	CH$_3$	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
505	CH$_2$-c-C$_3$H$_5$	CH$_3$	CH$_3$	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
506	CH$_2$CH$_2$CH$_3$	CH$_3$	CH$_3$	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
507	(S)(CH$_2$)$_3$		H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
508	(S)(CH$_2$)$_4$		H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
509	rac(CH$_2$)$_3$		H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
510	rac(CH$_2$)$_4$		H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
511	(R)(CH$_2$)$_3$		H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
512	(R)(CH$_2$)$_4$		H	H	CH$_3$	CH	CH	CH(CH$_3$)$_2$
513	CH$_2$CH=CH$_2$	H	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
514	CH$_2$-c-C$_3$H$_5$	H	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
515	CH$_2$CH$_2$CH$_3$	H	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
516	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
517	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
518	CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
519	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
520	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
521	CH$_2$-c-C$_3$H$_5$	rac- CH$_3$	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
522	CH$_2$CH$_3$	rac- CH$_3$	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
523	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
524	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
525	CH$_2$-c-C$_3$H$_5$	(R)CH$_3$	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
526	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
527	CH$_2$CH$_3$	(R)CH$_3$	H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
528	CH$_2$CH=CH$_2$	H	CH$_3$	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
529	CH$_2$-c-C$_3$H$_5$	H	CH$_3$	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
530	CH$_2$CH$_2$CH$_3$	H	CH$_3$	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
531	CH$_2$CH=CH$_2$	CH$_3$	H	CH$_3$	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
532	CH$_2$-c-C$_3$H$_5$	CH$_3$	H	CH$_3$	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
533	CH$_2$CH$_2$CH$_3$	CH$_3$	H	CH$_3$	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$

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No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^5
534	CH$_2$CH=CH$_2$	CH$_3$	CH$_3$	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
535	CH$_2$-c-C$_3$H$_5$	CH$_3$	CH$_3$	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
536	CH$_2$CH$_2$CH$_3$	CH$_3$	CH$_3$	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
537	(CH$_2$)$_3$		H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
538	(CH$_2$)$_4$		H	H	CH$_3$	C-Cl	CH	CH(CH$_3$)$_2$
539	CH$_2$CH=CH$_2$	H	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
540	CH$_2$-c-C$_3$H$_5$	H	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
541	CH$_2$CH$_2$CH$_3$	H	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
542	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
543	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
544	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
545	CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
546	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
547	CH$_2$-c-C$_3$H$_5$	rac- CH$_3$	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
548	CH$_2$CH$_3$	rac- CH$_3$	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
549	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
550	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
551	CH$_2$-c-C$_3$H$_5$	(R)CH$_3$	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
552	CH$_2$CH$_3$	(R)CH$_3$	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
553	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
554	CH$_2$CH=CH$_2$	H	CH$_3$	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
555	CH$_2$-c-C$_3$H$_5$	H	CH$_3$	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
556	CH$_2$CH$_2$CH$_3$	H	CH$_3$	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
557	CH$_2$CH=CH$_2$	CH$_3$	H	CH$_3$	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
558	CH$_2$-c-C$_3$H$_5$	CH$_3$	H	CH$_3$	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
559	CH$_2$CH$_2$CH$_3$	CH$_3$	H	CH$_3$	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
560	CH$_2$CH=CH$_2$	CH$_3$	CH$_3$	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
561	CH$_2$-c-C$_3$H$_5$	CH$_3$	CH$_3$	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
562	CH$_2$CH$_2$CH$_3$	CH$_3$	CH$_3$	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
563	(CH$_2$)$_3$		H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
564	(CH$_2$)$_4$		H	H	CH$_3$	CH	C-Cl	CH(CH$_3$)$_2$
565	CH$_2$CH=CH$_2$	H	H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
566	CH$_2$-c-C$_3$H$_5$	H	H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
567	CH$_2$CH$_2$CH$_3$	H	H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
568	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
569	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
570	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
571	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
572	CH$_2$-c-C$_3$H$_5$	rac- CH$_3$	H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
573	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
574	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$

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No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
575	CH$_2$-c-C$_3$H$_5$	(R)CH$_3$	H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
576	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
577	CH$_2$CH=CH$_2$	H	CH$_3$	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
578	CH$_2$-c-C$_3$H$_5$	H	CH$_3$	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
579	CH$_2$CH$_2$CH$_3$	H	CH$_3$	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
580	CH$_2$CH=CH$_2$	CH$_3$	H	CH$_3$	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
581	CH$_2$-c-C$_3$H$_5$	CH$_3$	H	CH$_3$	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
582	CH$_2$CH$_2$CH$_3$	CH$_3$	H	CH$_3$	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
583	CH$_2$CH=CH$_2$	CH$_3$	CH$_3$	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
584	CH$_2$-c-C$_3$H$_5$	CH$_3$	CH$_3$	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
585	CH$_2$CH$_2$CH$_3$	CH$_3$	CH$_3$	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
586	(CH$_2$)$_3$		H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
587	(CH$_2$)$_4$		H	H	CH$_3$	C-CH$_3$	CH	CH(CH$_3$)$_2$
588	CH$_2$CH=CH$_2$	H	H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
589	CH$_2$-c-C$_3$H$_5$	H	H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
590	CH$_2$CH$_2$CH$_3$	H	H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
591	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
592	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
593	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
594	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
595	CH$_2$-c-C$_3$H$_5$	rac- CH$_3$	H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
596	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
597	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
598	CH$_2$-c-C$_3$H$_5$	(R)CH$_3$	H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
599	CH$_2$CH$_2$CH$_3$	(R)CH$_3$	H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
600	CH$_2$CH=CH$_2$	H	CH$_3$	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
601	CH$_2$-c-C$_3$H$_5$	H	CH$_3$	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
602	CH$_2$CH$_2$CH$_3$	H	CH$_3$	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
603	CH$_2$CH=CH$_2$	CH$_3$	H	CH$_3$	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
604	CH$_2$-c-C$_3$H$_5$	CH$_3$	H	CH$_3$	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
605	CH$_2$CH$_2$CH$_3$	CH$_3$	H	CH$_3$	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
606	CH$_2$CH=CH$_2$	CH$_3$	CH$_3$	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
607	CH$_2$-c-C$_3$H$_5$	CH$_3$	CH$_3$	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
608	CH$_2$CH$_2$CH$_3$	CH$_3$	CH$_3$	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
609	(CH$_2$)$_3$		H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
610	(CH$_2$)$_4$		H	H	CH$_3$	CH	C-CH$_3$	CH(CH$_3$)$_2$
611	H	H	H	H	CH$_3$	CH	CH	c-C$_3$H$_5$
612	CH$_3$	H	H	H	CH$_3$	CH	CH	c-C$_3$H$_5$
613	CH$_2$CH$_3$	H	H	H	CH$_3$	CH	CH	c-C$_3$H$_5$
614	CH$_2$CH=CH$_2$	H	H	H	CH$_3$	CH	CH	c-C$_3$H$_5$
615	CH$_2$-c-C$_3$H$_5$	H	H	H	CH$_3$	CH	CH	c-C$_3$H$_5$

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No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^6
616	$CH_2CH_2CH_3$	H	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
617	H	(s)CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
618	CH_3	(s)CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
619	CH_2CH_3	(s)CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
620	$CH_2CH{=}CH_2$	(s)CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
621	$CH_2\text{-}c\text{-}C_3H_5$	(s)CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
622	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
623	CH_3	rac- CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
624	$CH_2CH{=}CH_2$	rac- CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
625	$CH_2\text{-}c\text{-}C_3H_5$	rac- CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
626	$CH_2CH_2CH_3$	rac- CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
627	CH_2CH_3	(R)CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
628	$CH_2CH{=}CH_2$	(R)CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
629	$CH_2\text{-}c\text{-}C_3H_5$	(R)CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
630	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
631	CH_3	H	CH_3	H	CH_3	CH	CH	$c\text{-}C_3H_5$
632	$CH_2CH{=}CH_2$	H	CH_3	H	CH_3	CH	CH	$c\text{-}C_3H_5$
633	$CH_2\text{-}c\text{-}C_3H_5$	H	CH_3	H	CH_3	CH	CH	$c\text{-}C_3H_5$
634	$CH_2CH_2CH_3$	H	CH_3	H	CH_3	CH	CH	$c\text{-}C_3H_5$
635	CH_3	CH_3	H	CH_3	CH_3	CH	CH	$c\text{-}C_3H_5$
636	$CH_2CH{=}CH_2$	CH_3	H	CH_3	CH_3	CH	CH	$c\text{-}C_3H_5$
637	$CH_2\text{-}c\text{-}C_3H_5$	CH_3	H	CH_3	CH_3	CH	CH	$c\text{-}C_3H_5$
638	$CH_2CH_2CH_3$	CH_3	H	CH_3	CH_3	CH	CH	$c\text{-}C_3H_5$
639	CH_3	CH_3	CH_3	H	CH_3	CH	CH	$c\text{-}C_3H_5$
640	$CH_2CH{=}CH_2$	CH_3	CH_3	H	CH_3	CH	CH	$c\text{-}C_3H_5$
641	$CH_2\text{-}c\text{-}C_3H_5$	CH_3	CH_3	H	CH_3	CH	CH	$c\text{-}C_3H_5$
642	$CH_2CH_2CH_3$	CH_3	CH_3	H	CH_3	CH	CH	$c\text{-}C_3H_5$
643	(s)$(CH_2)_3$		H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
644	(s)$(CH_2)_4$		H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
645	rac$(CH_2)_3$		H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
646	rac$(CH_2)_4$		H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
647	(R)$(CH_2)_3$		H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
648	(R)$(CH_2)_4$		H	H	CH_3	CH	CH	$c\text{-}C_3H_5$
649	$CH_2CH{=}CH_2$	H	H	H	CH_3	CH	C-Cl	$c\text{-}C_3H_5$
650	$CH_2\text{-}c\text{-}C_3H_5$	H	H	H	CH_3	CH	C-Cl	$c\text{-}C_3H_5$
651	$CH_2CH_2CH_3$	H	H	H	CH_3	CH	C-Cl	$c\text{-}C_3H_5$
652	$CH_2CH{=}CH_2$	(s)CH_3	H	H	CH_3	CH	C-Cl	$c\text{-}C_3H_5$
653	$CH_2\text{-}c\text{-}C_3H_5$	(s)CH_3	H	H	CH_3	CH	C-Cl	$c\text{-}C_3H_5$
654	CH_2CH_3	(s)CH_3	H	H	CH_3	CH	C-Cl	$c\text{-}C_3H_5$
655	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	CH	C-Cl	$c\text{-}C_3H_5$
656	$CH_2CH{=}CH_2$	rac- CH_3	H	H	CH_3	CH	C-Cl	$c\text{-}C_3H_5$

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^6
657	CH_2-c-C_3H_5	rac- CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
658	CH_2CH_3	rac- CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
659	$CH_2CH_2CH_3$	rac- CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
660	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
661	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
662	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
663	CH_2CH_3	(R)CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
664	$CH_2CH=CH_2$	H	H	H	CH_3	CH	C-CH_3	c-C_3H_5
665	CH_2-c-C_3H_5	H	H	H	CH_3	CH	C-CH_3	c-C_3H_5
666	$CH_2CH_2CH_3$	H	H	H	CH_3	CH	C-CH_3	c-C_3H_5
667	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
668	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
669	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
670	$CH_2CH=CH_2$	rac- CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
671	CH_2-c-C_3H_5	rac- CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
672	$CH_2CH_2CH_3$	rac- CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
673	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
674	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
675	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
676	$CH_2CH=CH_2$	H	H	H	CH_3	C-Cl	CH	c-C_3H_5
677	CH_2-c-C_3H_5	H	H	H	CH_3	C-Cl	CH	c-C_3H_5
678	$CH_2CH_2CH_3$	H	H	H	CH_3	C-Cl	CH	c-C_3H_5
679	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
680	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
681	CH_2CH_3	(s)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
682	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
683	$CH_2CH=CH_2$	rac- CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
684	CH_2-c-C_3H_5	rac- CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
685	$CH_2CH_2CH_3$	rac- CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
686	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
687	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
688	CH_2CH_3	(R)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
689	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
690	$CH_2CH=CH_2$	H	H	H	CH_3	C-CH_3	CH	c-C_3H_5
691	CH_2-c-C_3H_5	H	H	H	CH_3	C-CH_3	CH	c-C_3H_5
692	$CH_2CH_2CH_3$	H	H	H	CH_3	C-CH_3	CH	c-C_3H_5
693	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	C-CH_3	CH	c-C_3H_5
694	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	C-CH_3	CH	c-C_3H_5
695	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	C-CH_3	CH	c-C_3H_5
696	$CH_2CH=CH_2$	rac- CH_3	H	H	CH_3	C-CH_3	CH	c-C_3H_5
697	CH_2-c-C_3H_5	rac- CH_3	H	H	CH_3	C-CH_3	CH	c-C_3H_5

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^6
698	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	CH$_3$	C-CH$_3$	CH	c-C$_3$H$_5$
699	CH$_3$	H	H	H	CH$_3$	CH	CH	C$_2$H$_5$
700	CH$_2$CH=CH$_2$	H	H	H	CH$_3$	CH	CH	C$_2$H$_5$
701	CH$_2$-c-C$_3$H$_5$	H	H	H	CH$_3$	CH	CH	C$_2$H$_5$
702	CH$_2$CH$_2$CH$_3$	H	H	H	CH$_3$	CH	CH	C$_2$H$_5$
703	CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	CH	C$_2$H$_5$
704	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	CH$_3$	CH	CH	C$_2$H$_5$
705	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	CH$_3$	CH	CH	C$_2$H$_5$
706	CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	CH	C$_2$H$_5$
707	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	CH	C$_2$H$_5$
708	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	CH$_3$	CH	CH	C$_2$H$_5$
709	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	CH$_3$	CH	CH	C$_2$H$_5$
710	CH$_3$	(R)CH$_3$	H	H	CH$_3$	CH	CH	C$_2$H$_5$
711	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	CH$_3$	CH	CH	C$_2$H$_5$
712	CH$_2$-c-C$_3$H$_5$	(R)CH$_3$	H	H	CH$_3$	CH	CH	C$_2$H$_5$
713	CH$_2$CH=CH$_2$	H	CH$_3$	H	CH$_3$	CH	CH	C$_2$H$_5$
714	CH$_2$CH$_2$CH$_3$	H	CH$_3$	H	CH$_3$	CH	CH	C$_2$H$_5$
715	CH$_2$CH=CH$_2$	CH$_3$	H	CH$_3$	CH$_3$	CH	CH	C$_2$H$_5$
716	CH$_2$CH$_2$CH$_3$	CH$_3$	H	CH$_3$	CH$_3$	CH	CH	C$_2$H$_5$
717	CH$_2$CH=CH$_2$	CH$_3$	CH$_3$	H	CH$_3$	CH	CH	C$_2$H$_5$
718	CH$_2$CH$_2$CH$_3$	CH$_3$	CH$_3$	H	CH$_3$	CH	CH	C$_2$H$_5$
719	(s)(CH$_2$)$_3$		H	H	CH$_3$	CH	CH	C$_2$H$_5$
720	(s)(CH$_2$)$_4$		H	H	CH$_3$	CH	CH	C$_2$H$_5$
721	rac(CH$_2$)$_3$		H	H	CH$_3$	CH	CH	C$_2$H$_5$
722	rac(CH$_2$)$_4$		H	H	CH$_3$	CH	CH	C$_2$H$_5$
723	H	H	H	H	CH$_3$	CH	CH	CH=CH$_2$
724	CH$_3$	H	H	H	CH$_3$	CH	CH	CH=CH$_2$
725	CH$_2$CH$_3$	H	H	H	CH$_3$	CH	CH	CH=CH$_2$
726	CH$_2$CH=CH$_2$	H	H	H	CH$_3$	CH	CH	CH=CH$_2$
727	CH$_2$-c-C$_3$H$_5$	H	H	H	CH$_3$	CH	CH	CH=CH$_2$
728	CH$_2$CH$_2$CH$_3$	H	H	H	CH$_3$	CH	CH	CH=CH$_2$
729	H	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH=CH$_2$
730	CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH=CH$_2$
731	CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH=CH$_2$
732	CH$_2$CH=CH$_2$	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH=CH$_2$
733	CH$_2$-c-C$_3$H$_5$	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH=CH$_2$
734	CH$_2$CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH=CH$_2$
735	CH$_2$CH=CH$_2$	rac- CH$_3$	H	H	CH$_3$	CH	CH	CH=CH$_2$
736	CH$_2$CH$_2$CH$_3$	rac- CH$_3$	H	H	CH$_3$	CH	CH	CH=CH$_2$
737	CH$_2$CH$_3$	(s)CH$_3$	H	H	CH$_3$	CH	CH	CH=CH$_2$
738	CH$_2$CH=CH$_2$	(R)CH$_3$	H	H	CH$_3$	CH	CH	CH=CH$_2$

30

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
739	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
740	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
741	$CH_2CH=CH_2$	H	CH_3	H	CH_3	CH	CH	$CH=CH_2$
742	$CH_2CH_2CH_3$	H	CH_3	H	CH_3	CH	CH	$CH=CH_2$
743	$CH_2CH=CH_2$	CH_3	H	CH_3	CH_3	CH	CH	$CH=CH_2$
744	$CH_2CH_2CH_3$	CH_3	H	CH_3	CH_3	CH	CH	$CH=CH_2$
745	$CH_2CH=CH_2$	CH_3	CH_3	H	CH_3	CH	CH	$CH=CH_2$
746	$CH_2CH_2CH_3$	CH_3	CH_3	H	CH_3	CH	CH	$CH=CH_2$
747	$(CH_2)_3$		H	H	CH_3	CH	CH	$CH=CH_2$
748	$(CH_2)_4$		H	H	CH_3	CH	CH	$CH=CH_2$

rac: racemate; (S): S configuration; (R) R configuration.

Other examples of compounds according to the invention are the compounds of the general formulae Ia.3, Ib, Ic, Id, Ie and If:

5

(Ia.3)

(Ib)

(Ic)

(Id)

31
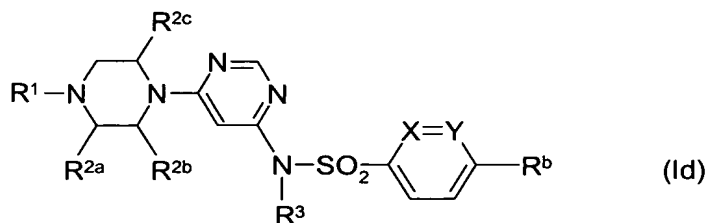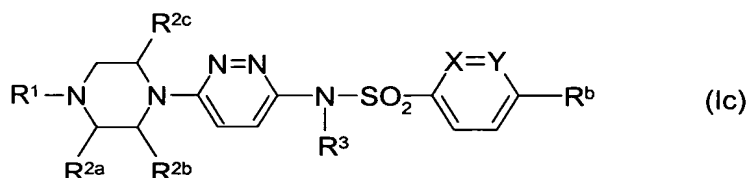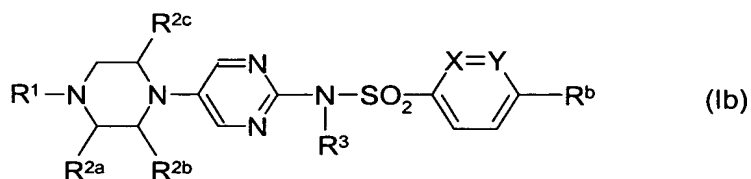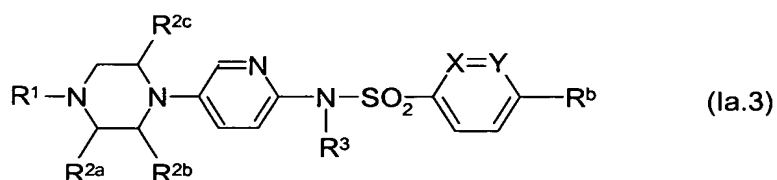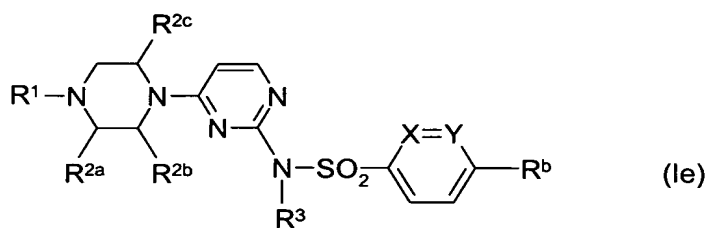
$$\text{(Ie)}$$
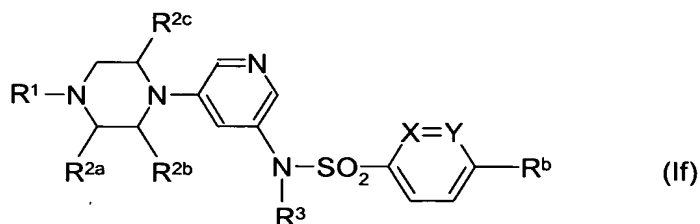
$$\text{(If)}$$

in which R^1, R^{2a}, R^{2b}, R^{2c}, R^3, X, Y and R^b have the meanings specified in one line in Table 1.

5 Among the compounds of the general formula I, preference is also given to the compounds of the general formula Ig
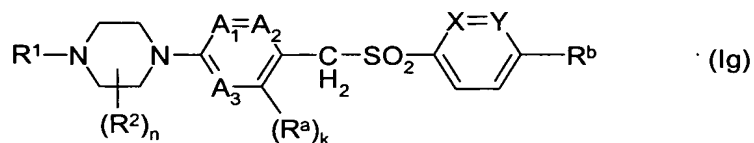
$$\text{(Ig)}$$

10 in which n, k, R^1, R^2, R^a, R^b, A^1, A^2, A^3, X and Y have the meanings given for formula Ia.

Among the compounds of the general formula I, preference is also given to the compounds of the general formula Ih
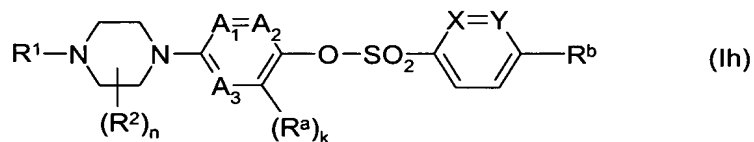
$$\text{(Ih)}$$

15

in which n, k, R^1, R^2, R^a, R^b, A^1, A^2, A^3, X and Y have the meanings given for formula Ia.

Among the compounds of general formulae Ig and Ih, preference is given to the compounds
20 of general formula Ig.1, Ig.2, Ih.1 and Ih.2

32

(Ig.1: R = CH$_2$)

(Ih.1: R = O)

(Ig.2: R = CH$_2$)

(Ih.2: R = O)
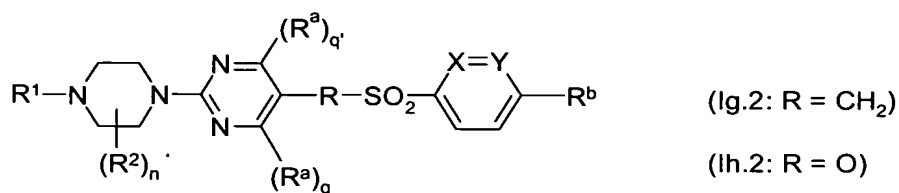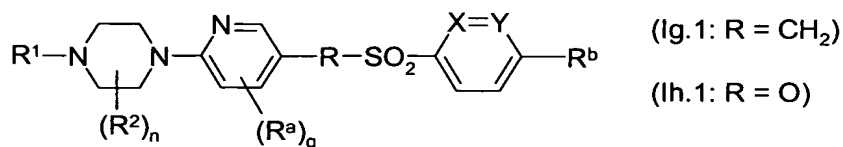
in which n, q, q', X, Y, R^1, R^2, R^a and R^b have the meanings mentioned previously for formulae Ia.1 and Ia.2 and R is CH$_2$ (compounds Ig.1 and Ig.2) or O (compounds Ih.1 or Ih.2).

5

Examples of compounds of the formula Ig.1 and Ih.1 are the compounds of the following general formulae Ig.1a, Ig.1b, Ig.1c, Ig.1d, Ig.1e, Ig.1f, Ig.1g, Ig.1h,.Ig.1k, Ih.1a, Ih.1b, Ih.1c, Ih.1h, Ih.1e, Ih.1f, Ih.1g, Ih.1h and Ih.1k:
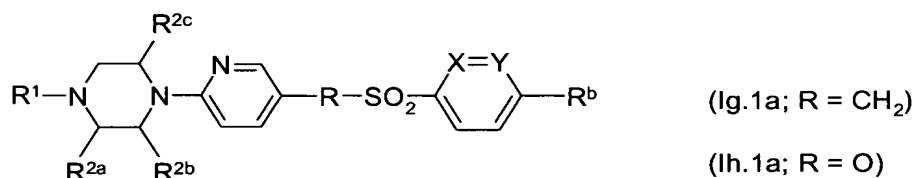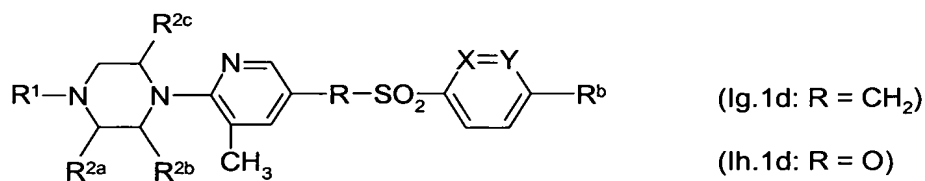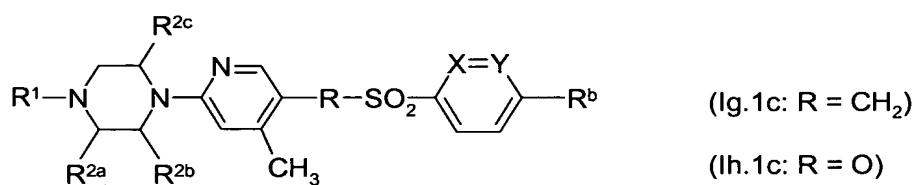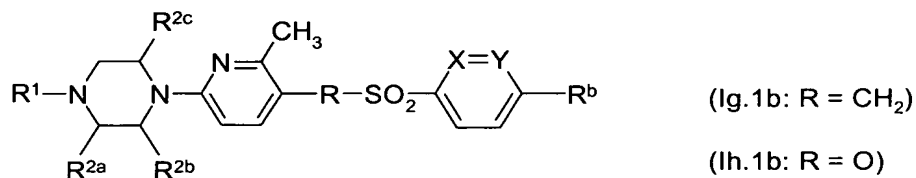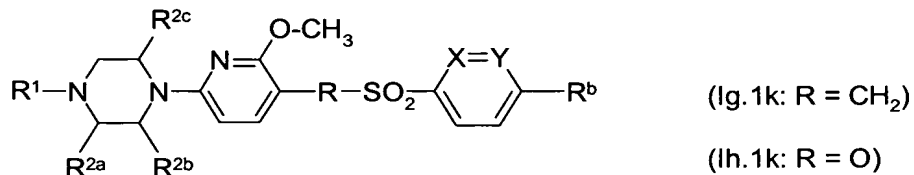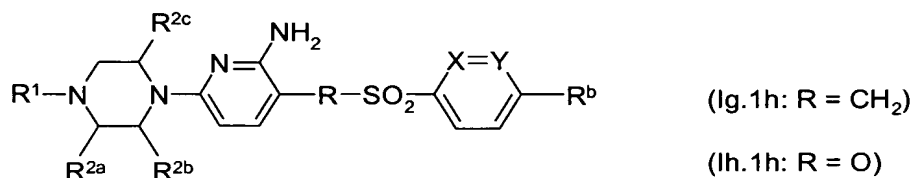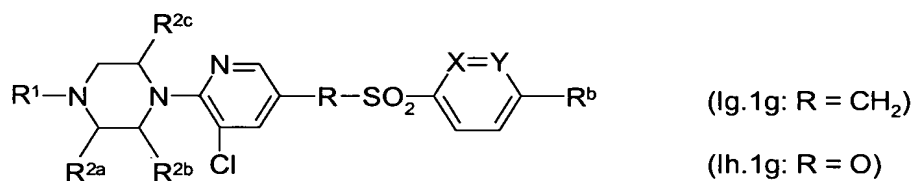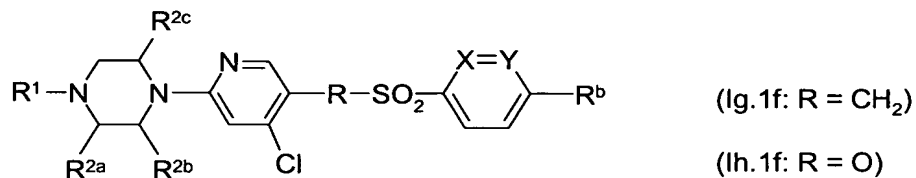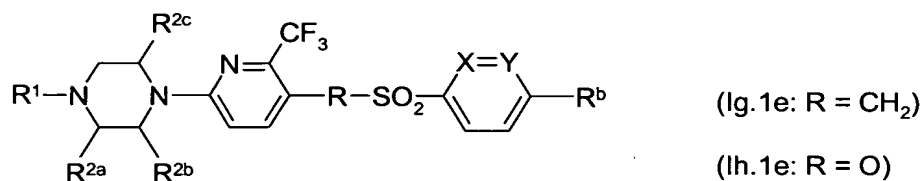
(Ig.1a; R = CH$_2$)

(Ih.1a; R = O)

10

(Ig.1b: R = CH$_2$)

(Ih.1b: R = O)

(Ig.1c: R = CH$_2$)

(Ih.1c: R = O)

(Ig.1d: R = CH$_2$)

(Ih.1d: R = O)

33

(Ig.1e: R = CH₂)

(Ih.1e: R = O)

(Ig.1f: R = CH₂)

(Ih.1f: R = O)

(Ig.1g: R = CH₂)

(Ih.1g: R = O)

(Ig.1h: R = CH₂)

(Ih.1h: R = O)

(Ig.1k: R = CH₂)

(Ih.1k: R = O)

5

in which R^1, R^{2a}, R^{2b}, R^{2c}, X, Y and R^b have the meanings specified in one of the lines 1 to 474 in Table 1.

10

Examples of compounds of the formula Ig.1 and Ih.1 are the compounds of the following general formulae Ig.2a, Ig.2b, Ig.2c, Ig.2d, Ig.2e, Ih.2a, Ih.2b, Ih.2c, Ih.2d and Ih.2e:

(Ig.2a: R = CH₂)

(Ih.2a: R = O)

34

$$R^1-N\underset{R^{2a}\quad R^{2b}}{\overset{R^{2c}}{\bigvee}}N-\underset{N}{\overset{CF_3}{\bigvee}}-R-SO_2-\underset{X=Y}{\bigcirc}-R^b$$

(Ig.2b: R = CH$_2$)

(Ih.2b: R = O)

$$R^1-N\underset{R^{2a}\quad R^{2b}}{\overset{R^{2c}}{\bigvee}}N-\underset{N}{\overset{CH_3}{\bigvee}}-R-SO_2-\underset{X=Y}{\bigcirc}-R^b$$

(Ig.2c: R = CH$_2$)

(Ih.2c: R = O)

$$R^1-N\underset{R^{2a}\quad R^{2b}}{\overset{R^{2c}}{\bigvee}}N-\underset{N}{\overset{O-CH_3}{\bigvee}}-R-SO_2-\underset{X=Y}{\bigcirc}-R^b$$

(Ig.2d: R = CH$_2$)

(Ih.2d: R = O)

$$R^1-N\underset{R^{2a}\quad R^{2b}}{\overset{R^{2c}}{\bigvee}}N-\underset{N}{\overset{NH_2}{\bigvee}}-R-SO_2-\underset{X=Y}{\bigcirc}-R^b$$
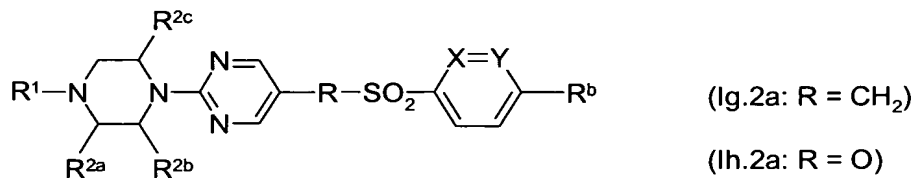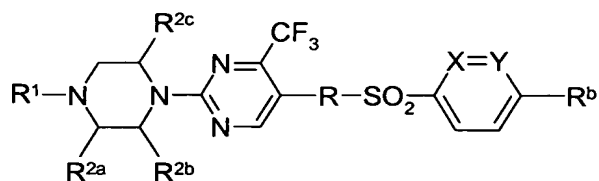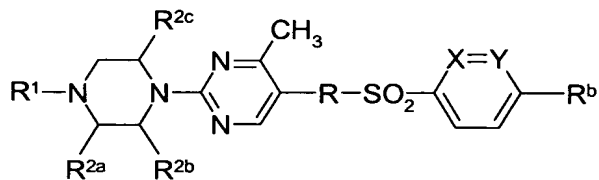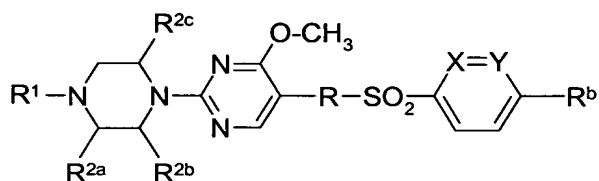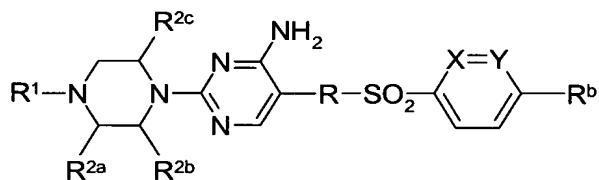
(Ig.2e: R = CH$_2$)

(Ih.2e: R = O)

5

in which R^1, R^{2a}, R^{2b}, R^{2c}, X, Y and R^b have the meanings specified in one of the lines 1 to 474 in Table 1.

The compounds I according to the invention are prepared in analogy with methods known
10   from the literature. An important approach to the compounds according to the invention with R being O or N-R^3 is offered by the reaction of a hetarylcompound II with an arylsulfonic acid derivative III as depicted in scheme 1.

Scheme 1:
15

$$R^1-N\underset{(R^2)_n}{\bigvee}N-Q-R-H \quad + \quad X-SO_2-Ar \quad \longrightarrow \quad I: R = O, N-R^3$$

(II)   (III)

35
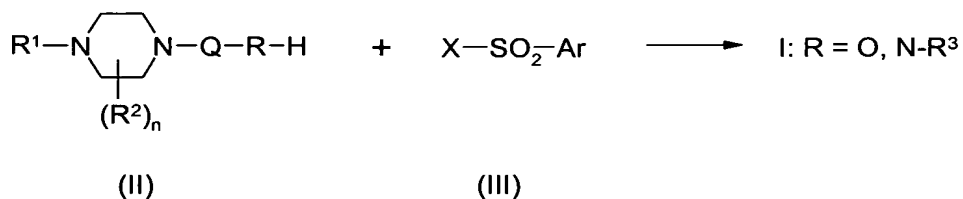
In scheme 1, n, R^1, R^2, R^3, Ar and Q have the previously mentioned meanings. R is O or N-R^3. X is a nucleophilically displaceable leaving group, in particular a halogen atom and, especially, chlorine or bromine. The reaction depicted in scheme 1 takes place under the reaction conditions which are customary for preparing arylsulfonamide compounds or arylsulfonic

5   esters, respectively, and which are described, for example, in J. March, Advanced Organic Chemistry, 3rd edition, John Wiley & Sons, New York, 1985 p 444 and the literature cited therein, European J. Org. Chem. 2002 (13), pp. 2094-2108, Tetrahedron 2001, 57 (27) pp. 5885-5895, Bioorganic and Medicinal Chemistry Letters, 2000, 10(8), pp. 835-838 and Synthesis 2000 (1), pp. 103-108.

10

The reaction customarily takes place in an inert solvent, for example in an ether, such as diethyl ether, diisopropyl ether, methyl tert-butyl ether or tetrahydrofuran, a halohydrocarbon, such as dichloromethane, an aliphatic or cycloaliphatic hydrocarbon, such as pentane, hexane or cyclohexane, or an aromatic hydrocarbon, such as toluene, xylene, cumene and the

15   like, or in a mixture of the abovementioned solvents.

The reaction of II with III is customarily carried out in the presence of an auxiliary base. Suitable bases are inorganic bases, such as sodiumcarbonate or potassiumcarbonate, or sodiumhydrogencarbonate or potassiumhydrogencarbonate, and organic bases, for example

20   trialkylamines, such as triethylamine, or pyridine compounds, such as pyridine, lutidine and the like. The latter compounds can at the same time serve as solvents. The auxiliary base is customarily employed in at least equimolar quantities, based on the amine compound II.

The compounds of the general formula II are known per se or, in case R is N-R^{3a}, can be

25   prepared in the manner shown in schemes 2.

Scheme 2:

30
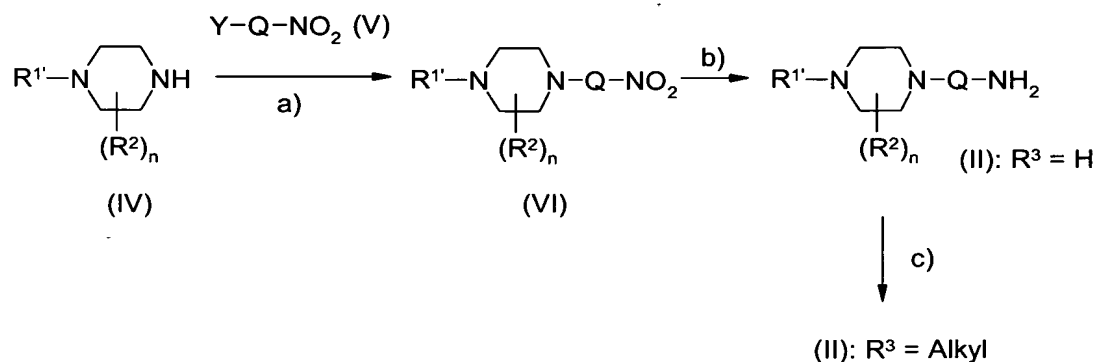
In scheme 2, n, R^2 and Q have the previously mentioned meanings. $R^{1'}$ has the meanings different from hydrogen which are specified for R^1 or is a suitable protecting group. Suitable

protecting groups are disclosed, for example, in P. Kocienski, Protecting Groups, Thieme-Verlag, Stuttgart 2000, Chapter 6. Y is a nucleophilically displaceable leaving group, in particular a halogen atom, e.g. chlorine or bromine, or an alkylsulfonyl group, e.g. methylsulfonyl.

5

The reaction depicted in step a) in scheme 2 takes place under the reaction conditions which are customary for a nucleophilic substitution on an aromatic radical and which are described, for example, in Tetrahedron 1999, 55(33), pp. 10243-10252, J. Med. Chem. 1997, 40(22), pp. 3679-3686 and Synthetic Communications, 1993, 23(5), pp. 591-599. Where appropri-
10   ate, it can be advantageous to convert a ring nitrogen atom in the Q group into its N-oxide (see, for example, Angew. Chem. Int. Ed. Engl.,2002 41(11), pp. 1937-1940, J. Med. Chem. 1985, 28(2), pp. 248-252 and Tetrahedron Lett. 2002 43(17) pp. 3121-3123). This approach has proved to be of value, in particular, for preparing compounds I in which Q is a pyridin-2,4-diyl group. In connection with the subsequent reduction of the nitro group in VI (step b),
15   the N-oxide group is also reduced. For this, the reduction is carried out, for example, in the presence of indium salts.

If 5-bromonitropyridine is used as compound V in step a) in accordance with scheme 2, the coupling is also achieved under palladium catalysis in the presence of an auxiliary base, for
20   example an alkali metal carbonate such as cesium carbonate. Particularly suitable palladium catalysts in this connection are palladium(0) compounds or palladium compounds which are able to form a palladium(0) compound under reaction conditions, e.g. palladium dichloride, tetrakis(triphenylphosphine)palladium(0), tris(dibenzylideneacetone)dipalladium(0), advantageously in combination with phosphine ligands, e.g. triarylphosphines, such as triphenyl-
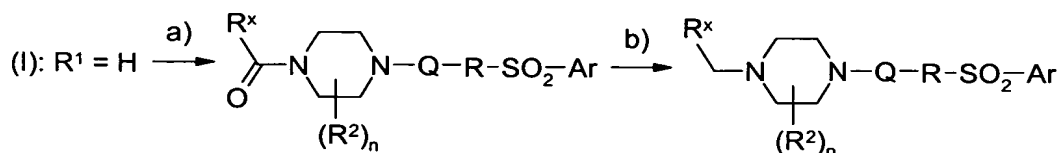25   phosphine, trialkylphosphines, such as tributylphosphine, and cycloalkylphosphines, such as tricyclohexylphosphine, and, especially, using phosphine chelate ligands, such as 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl. The conditions which are required for reactions of this nature are described, for example, in Tetrahedron Lett. 2001, 42(22), p. 3681 and Tetrahedron Lett. 2002, 43(12), pp. 2171-2173.
30

In step b), the nitro group in VI is reduced to the NH_2 group in II. Subsequently, in step c), the NH_2 group can be converted into a $-NR^{3'}H$ group, in which $R^{3'}$ has the meanings different from hydrogen which are specified for R^3.

35   The reaction conditions which are required for step b) correspond to the customary conditions for reducing aromatic nitro groups which have been described extensively in the literature (see, for example, J. March, Advanced Organic Chemistry, 3rd ed., J. Wiley & Sons, New-York, 1985, p. 1183 and the literature cited in this reference).

The reduction is achieved, for example, by reacting the nitro compound VII with a metal such as iron, zinc or tin under acidic reaction conditions, i.e. using nascent hydrogen, or using a complex hydride such as lithium aluminum hydride or sodium borohydride, preferably in the presence of transition metal compounds of nickel or cobalt such as $NiCl_2(P(phenyl)_3)_2$, or

5     $CoCl_2$,(see Ono et al. Chem. Ind. (London), 1983 p.480), or using $NaBH_2S_3$ (see Lalancette et al. Can. J. Chem. 49, 1971, p. 2990), with it being possible to carry out these reductions, depending on the given reagent, in substance or in a solvent or diluent. Alternatively, the reduction of VI to II can be carried out with hydrogen in the presence of a transition metal catalyst, e.g. using hydrogen in the presence of catalysts based on platinum, palladium,

10   nickel, ruthenium or rhodium. The catalysts can contain the transition metal in elemental form or in the form of a complex compound, of a salt or of an oxide of the transition metal, with it being possible, for the purpose of modifying the activity, to use customary coligands, e.g. organic phosphine compounds, such as triphenylphosphine, tricyclohexylphosphine or tri-n-butylphosphines or phosphites. The catalyst is customarily employed in quantities of

15   from 0.001 to 1 mol per mol of compound VI, calculated as catalyst metal. In a preferred variant, the reduction is effected using tin(II) chloride in analogy with the methods described in Bioorganic and Medicinal Chemistry Letters, 2002, 12(15), pp. 1917-1919 and J. Med. Chem. 2002, 45(21), pp. 4679-4688. The reaction of VI with tin(II) chloride is preferably carried out in an inert organic solvent, preferably an alcohol such as methanol, ethanol, isopro-

20   panol or butanol.

Reducing VI results in compounds II in which R^3 is hydrogen. Customary methods can then be used to react these compounds with an alkylating agent $R^{3'}$-X, in which $R^{3'}$ is C_1-C_4-alkyl and X is a nucleophilically displaceable leaving group (e.g. halogen, such as chlorine, bro-

25   mine or iodine), resulting in a compound II in which R^3 = alkyl (step c). The reaction conditions which are required for this are disclosed, for example, in WO 02/83652, Tetrahedron 2000, 56(38) pp. 7553-7560 and Synlett. 2000 (4), pp. 475-480.

The compound I can also be prepared by the route depicted in scheme 3:

30

Scheme 3:

     (VII)   (VIII)
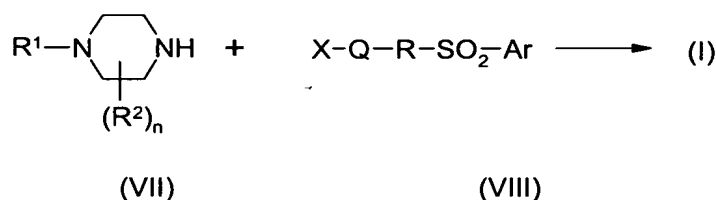
35   In scheme 3, n, R, R^1, R^2, Ar and Q have the previously mentioned meanings. Y is a nucleo-philically displaceable leaving group, in particular a halogen atom, e.g. chlorine or bromine,

38

or an alkylsulfonyl group, e.g. methylsulfonyl. The reaction of VII with VIII, as depicted in scheme 3, takes place under the reaction conditions specified for scheme 2, step a). Compounds of the general formulae VII and VIII are known or can be prepared in analogy with the methods known from the literature. Compounds or the formula VIII, wherein R is N-R^3 or

5   an oxygen atom can be prepared by amidation of the the corresponding aminocompound X-Q-NHR^3 (or esterification of the corresponding hydroxycompound X-Q-OH) with a sulfonyl-halide, especiall with a sulfonylchloride of the formula Z-SO$_2$-Ar, wherein Z is halogen, especially chlorine or bromine, according to standard methods of organic chemistry (see e.g. J. March, Advanced Organic Chemistry, 3rd edition, John Wiley & Sons, New York, 1985 p 444

10   and the literature cited therein).

Compounds of general formula I, in which R^1 is an allyl group, can be converted into compounds possessing different R^1 substituents using the synthetic route shown in scheme 4.

15   Scheme 4:

(I): R^1 = CH$_2$-CH=CH$_2$

(I): R^1 = H

b)

(I): R^1 = alkyl, cycloalkyl,
cycloalkylalkyl, alkenyl
haloalkyl, alkynyl
alkoxyalkyl, hydroxyalkyl
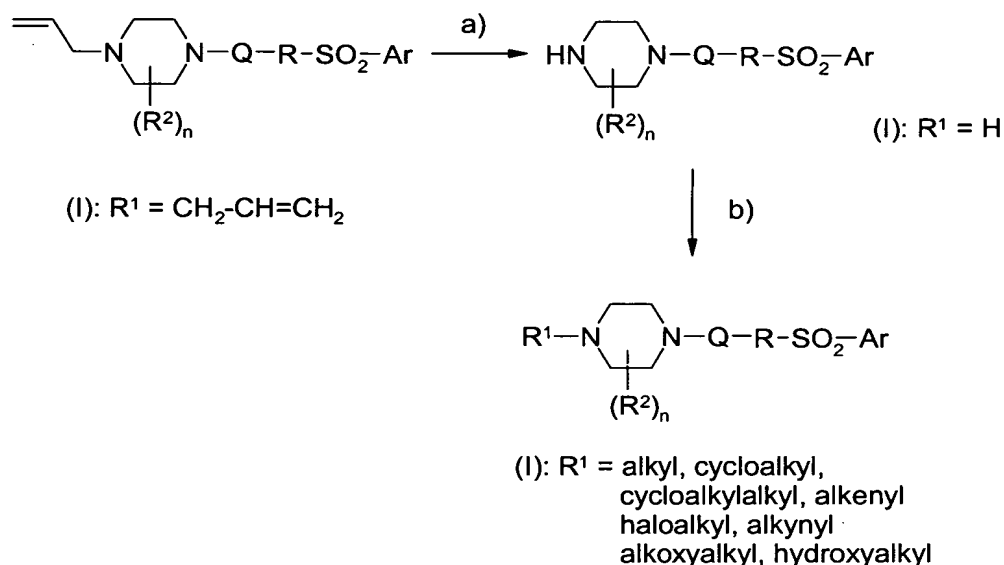
In scheme 4, n, R, R^2, Ar and Q have the previously mentioned meanings. The elimination of

20   the allyl group, as depicted in step a) in scheme 4, is achieved, for example, by reacting I [R^1 = allyl] with an allyl trapping agent, such as mercaptobenzoic acid or 1,3-dimethylbarbituric acid, in the presence of catalytic quantities of palladium (0) compounds or palladium compounds which are able to form a palladium(0) compound under reaction conditions, e.g. palladium dichloride, tetrakis(triphenylphosphine)palladium(0) or

25   tris(dibenzylideneacetone)dipalladium(0), advantageously in combination with phosphine ligands, e.g. triarylphosphines, such as triphenylphosphine, trialkylphosphines, such as tribu-

tylphosphine, and cycloalkylphosphines, such as tricyclohexylphosphine, and especially with phosphine chelate ligands, such as 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl or 1,4-bis(diphenylphosphino)butane, using methods known from the literature (with regard to eliminating N-allyl in the presence of mercaptobenzoic acid, see WO 94/24088; with regard

5 to eliminating in the presence of 1,3-dimethylbarbituric acid, see J. Am. Chem. Soc. 2001, 123 (28), pp. 6801-6808 and J. Org. Chem 2002, 67(11) pp. 3718-3723). Alternatively, the elimination of N-allyl, as depicted in scheme 4 step a), can also be effected by reacting in the presence of rhodium compounds, such as tris(triphenylphosphine)chlororhodium(I), using methods known from the literature (see J. Chem. Soc., Perkin Transaction I: Organic and

10 Bio-Organic Chemistry 1999 (21) pp. 3089-3104 and Tetrahedron Asymmetry 1997, 8(20), pp. 3387 - 3391).

The resulting piperazine compound I [R^1 = H] can then be reacted, in a known manner, in the sense of an alkylation, with a compound R^1-X. In this compound, R^1 is C_1-C_4-alkyl, C_3-

15 C_6-cycloalkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl or C_3-C_6-cycloalkyl-C_1-C_4-alkyl and X is a nucleophilically displaceable leaving group, e.g. halogen, trifluoroacetate, alkylsulfonate, arylsulfonate, alkyl sulfate and the like. The reaction conditions which are required for the alkylation in step b) have been adequately disclosed, e.g. in Bioorganic and Medicinal Chemistry Lett. 2002, 12(7), pp. 2443-2446 and also 2002, 12(5), pp. 1917-1919.

20

The conversion, as depicted in scheme 4, step b), of the piperazine compound I [R^1 = H] obtained in step a) can also be achieved, in the sense of a reductive amination, by reacting I [R^1 = H] with a suitable ketone or aldehyde in the presence of a reducing agent, e.g. in the presence of a borohydride such as sodium borohydride, sodium cyanoborohydride or so-

25 dium triacetoxyborohydride. The skilled person is familiar with the reaction conditions which are required for a reductive amination, e.g. from Bioorganic and Medicinal Chemistry Lett. 2002, 12(5), pp. 795-798 and 12(7) pp. 1269-1273.

The conversion, as depicted in scheme 4, step b), of the piperazine compound I [R^1 = H]

30 obtained in step a) can also be achieved by successive acylation and subsequent reduction of the acylation product, using the method depicted in scheme 4a:

Scheme 4a:

40

$$(I): R^1 = H \xrightarrow{a)} \underset{\underset{(R^2)_n}{O}}{R^x}C-N\underset{}{\overbrace{}}N-Q-R-SO_2\text{-}Ar \xrightarrow{b)} R^x\text{-}N\underset{(R^2)_n}{\overbrace{}}N-Q-R-SO_2\text{-}Ar$$

R^x = alkyl, cycloalkyl,
cycloalkylalkyl, alkenyl
haloalkyl, alkynyl
alkoxyalkyl, hydroxyalkyl

In scheme 4a, n, R, R^2, Ar and Q have the previously mentioned meanings. The acylation in
step a) and the reduction in step b) are effected using standard methods of organic chemis-
5   try as are described, for example, in J. March, Advanced Organic Chemistry, 3rd ed. J. Wiley
& Sons, New York 1985, p.370 and 373 (acylation) and p. 1099 f. and in the literature cited
in this publication (with regard to acylation, see also Synth. Commun. 1986, 16, p. 267, and
with regard to reduction, see also J. Heterocycl. Chem. 1979, 16, p. 1525).

10   In compounds of the general formula I which carry a halogen atom, in particular bromine or
iodine, on the aromatic radical Ar, the halogen atom can be converted into an alkyl, alkenyl,
cycloalkyl, alkynyl or cycloalkylalkyl group using methods which are known per se. The con-
version is achieved by coupling the halo compound I to an alkyl-, alkenyl-, alkynyl-, cycloal-
kyl- or cycloalkylalkyl-boronic acid compound under the conditions of a Suzuki coupling as is
15   described, for example, in Tetrahedron Lett. 2002, 43, pp. 6987-6990; Chem. Rev. 1995, 95,
pp. 2457-2483 and J. Org. Chem. 66(21) (2001), pp. 7124-7128.

Compounds of the formula I, wherein R is $CR^{3a}R^{3b}$, can be also prepared by the synthetic
route illustrated in scheme 5:

20

$$R^1\text{-}N\underset{(R^2)_n}{\overbrace{}}N-Q-CR^{3a}R^{3b}\text{-}L \xrightarrow{Ar\text{-}SH} R^1\text{-}N\underset{(R^2)_n}{\overbrace{}}N-Q-CR^{3a}R^{3b}\text{-}S\text{-}Ar \xrightarrow{[Ox]} I: R = CR^{3a}R^{3b}$$

(IX)   (X)
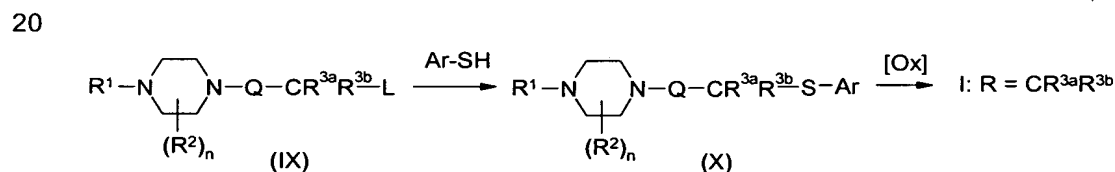
In scheme 5, n, R^1, R^2, Q, R^{3a}, R^{3b} and Ar are as defined above. L is a nucleophilically dis-
placeable leaving group, in particular a halogen atom such as chlorine or bromine or a sul-
25   fonate group, e.g. a C_1-C_4-alkylsulfonate such as methanesulfonate or an arylsulfonate such
benzenesulfoante or tosylate (toluene sulfonate). L may also be OH, when R^{3a}, R^{3b} are dif-
ferent from hydrogen.The reaction depicted in the first step of scheme 5 takes place under
the reaction conditions which are customary for preparing arylsulfide compounds which are
described, for example, in J. March, Advanced Organic Chemistry, 3rd edition, John Wiley &
30   Sons, New York, 1985 p 360 to 362, and in the literature cited therein.

41

In the second step of scheme 5 the sulfide X obtained in the first step is oxidized to the corresponding sulfone I (R = $CR^{3a}R^{3b}$) under reaction conditions which are customary for preparing arylsulfone compounds from the corresponding arylsulfides and which are described,

5   for example, in J. March, Advanced Organic Chemistry, 3rd edition, John Wiley & Sons, New York, 1985 p 1089 f. and in the literature cited therein.

The compounds of the formula IX are known in the art or can be prepared according to the method depicted in scheme 6:

10
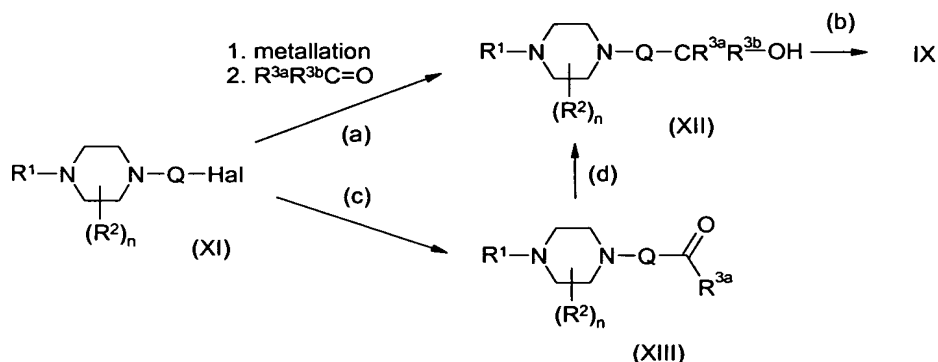
In scheme 6, n, R^1, R^2, Q, R^{3a}, R^{3b} and Ar are as defined above. Hal is halogen, especially chlorine, bromine or iodine. In step (a) of scheme 6 the halogen compound XI is first metal-

15   lized, i.e. converted into the corresponding lithium compound or magnesium compound by standard methods of organic chemistry and the thus obtained metal compound is reacted with an aldehyde or ketone to obtain the alcohol XII (see e.g. Tetrahedron 2003, 59 (24), 4303-4308). In step (b) he OH group of XII is then converted into a suitable leaving group, e.g. into a halogen atom by reaction with thionylhalide such as $SOCl_2$ or phosphorylhalide

20   such as $POCl_3$, or into an alkylsulfonate or arylsulfonate by reaction with an alkylsulfonylhalide such as methanesulfonylchloride or with an arylsulfonylhalide such as toluoenesulfonylchloride (see e.g. J. Med. Chem. 1985, 28 (12), 1790-1796).

Alternatively the halogen compound XI is converted into the carbonyl compound XIII (step c,

25   see e.g. J. Med. Chem. 1987, 30 (8), 1494-1497), which is then reduced (R^{3b} = H) or reacted with an alkylgrignard R^{3b}-Mg-X (X = halogen, e.g. Cl or Br) to obtain the alcohol XII (step (d), see e.g. J. Org. Chem. 2003, 68 (9), 3736-3738).

If not otherwise indicated, the above-described reactions are generally carried out in a sol-

30   vent at temperatures between room temperature and the boiling temperature of the solvent employed. Alternatively, the activation energy which is required for the reaction can be introduced into the reaction mixture using microwaves, something which has proved to be of

value, in particular, in the case of the reactions catalyzed by transition metals (with regard to reactions using microwaves, see Tetrahedron 2001, 57, p. 9199 ff. p. 9225 ff. and also, in a general manner, "Microwaves in Organic Synthesis", André Loupy (Ed.), Wiley-VCH 2002.

5   Examples of solvents which can be used are ethers, such as diethyl ether, diisopropyl ether, methyl tert-butyl ether or tetrahydrofuran, aprotic polar solvent, such as dimethylformamide, dimethyl sulfoxide, dimethoxyethane, and acetonitrile, aromatic hydrocarbons, such as toluene and xylene, ketones, such as acetone or methyl ethyl ketone, halohydrocarbons, such as dichloromethane, trichloromethane and dichloroethane, esters, such as ethyl acetate and
10   methyl butyrate, carboxylic acids, such as acetic acid or propionic acid, and alcohols, such as methanol, ethanol, n-propanol, isopropanol and butanol.

If desired, it is possible for a base to be present in order to neutralize protons which are released in the reactions. Suitable bases include inorganic bases, such as sodium carbonate,
15   potassium carbonate, sodium hydrogen carbonate or potassium hydrogen carbonate, and, in addition, alkoxides, such as sodium methoxide or sodium ethoxide, alkali metal hydrides, such as sodium hydride, and also organometallic compounds, such as butyllithium compounds or alkylmagnesium compounds, or organic nitrogen bases, such as triethylamine or pyridine. The latter compounds can at the same time serve as solvents.
20

The crude product is isolated in a customary manner, for example by filtering, distilling off the solvent or extracting from the reaction mixture, etc. The resulting compounds can be purified in a customary manner, for example by means of recrystallizing from a solvent, by means of chromatography or by means of converting into an acid addition salt.
25

The acid addition salts are prepared in a customary manner by mixing the free base with a corresponding acid, where appropriate in solution in an organic solvent, for example a lower alcohol, such as methanol, ethanol or propanol, an ether, such as methyl tert-butyl ether or diisopropyl ether, a ketone, such as acetone or methyl ethyl ketone, or an ester, such as
30   ethyl acetate.

The compounds according to the invention of the formula I are highly selective dopamine D_3 receptor ligands which, because of their low affinity for other receptors such as D_1 receptors, D_4 receptors, α1-adrenergic and/or α2-adrenergic receptors, muscarinergic receptors, his-
35   tamine receptors, opiate receptors and, in particular, dopamine D_2 receptors, give rise to fewer side-effects than do the classic neuroleptics, which are D_2 receptor antagonists.

The high affinity of the compounds according to the invention for D_3 receptors is reflected in very low in-vitro K_i values of as a rule less than 100 nM (nmol/l), in particular less than 50 nM

and, in particular, of less than 10 nM. The displacement of [^{125}I]-iodosulpride can, for example, be used in receptor binding studies for determining binding affinities for D_3 receptors.

5 The selectivity $K_i(D_2)/K_i(D_3)$ of the compounds according to the invention is as a rule at least 10, preferably at least 30, even better at least 50 and particularly advantageously at least 100. The displacement of [^{3}H]SCH23390, [^{125}I] iodosulpride or [^{125}I] spiperone can be used, for example, for carrying out receptor binding studies on D_1, D_2 and D_4 receptors.

10 Because of their binding profile, the compounds can be used for treating diseases which respond to dopamine D_3 ligands, i.e. they are effective for treating those disturbances or diseases in which exerting an influence on (modulating) the dopamine D_3 receptors leads to an improvement in the clinical picture or to the disease being cured. Examples of these diseases are disturbances or diseases of the central nervous system.

15 Disturbances or diseases of the central nervous system are understood as meaning disturbances which affect the spinal chord and, in particular, the brain. Within the meaning of the invention, the term "disturbance" denotes anomalies which are as a rule regarded as being pathological conditions or functions and which can manifest themselves in the form of particular signs, symptoms and/or malfunctions. While the treatment according to the invention 20 can be directed toward individual disturbances, i.e. anomalies or pathological conditions, it is also possible for several anomalies, which may be causatively linked to each other, to be combined into patterns, i.e. syndromes, which can be treated in accordance with the invention.

25 The disturbances which can be treated in accordance with the invention are, in particular, psychiatric and neurological disturbances. These disturbances include, in particular, organic disturbances, including symptomatic disturbances, such as psychoses of the acute exogenous reaction type or attendant psychoses of organic or exogenous cause, e.g., in association with metabolic disturbances, infections and endocrinopathogies; endogenous psycho- 30 ses, such as schizophrenia and schizotype and delusional disturbances; affective disturbances, such as depressions, mania and/or manic-depressive conditions; and also mixed forms of the above-described disturbances; neurotic and somatoform disturbances and also disturbances in association with stress; dissociative disturbances, e.g. loss of consciousness, clouding of consciousness, double consciousness and personality disturbances; dis- 35 turbances in attention and waking/sleeping behavior, such as behavioral disturbances and emotional disturbances whose onset lies in childhood and youth, e.g. hyperactivity in children, intellectual deficits, in particular attention disturbances (attention deficit disorders), memory disturbances and cognitive disturbances, e.g. impaired learning and memory (impaired cognitive function), dementia, narcolepsy and sleep disturbances, e.g. restless legs 40 syndrome; development disturbances; anxiety states, delirium; sexlife disturbances, e.g.

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impotence in men; eating disturbances, e.g. anorexia or bulimia; addiction; and other un-
specified psychiatric disturbances.

5   The disturbances which can be treated in accordance with the invention also include Parkin-
son's disease and epilepsy and, in particular, the affective disturbances connected thereto.

The addiction diseases include psychic disturbances and behavioral disturbances which are
caused by the abuse of psychotropic substances, such as pharmaceuticals or narcotics, and
also other addiction diseases, such as addiction to gaming (impulse control disorders not
10   elsewhere classified). Examples of addictive substances are: opioids (e.g. morphine, heroin
and codeine), cocaine; nicotine; alcohol; substances which interact with the GABA chloride
channel complex, sedatives, hypnotics and tranquilizers, for example benzodiazepines; LSD;
cannabinoids; psychomotor stimulants, such as 3,4-methylenedioxy-N-methylamphetamine
(ecstasy); amphetamine and amphetamine-like substances such as methylphenidate and
15   other stimulants including caffeine. Addictive substances which come particularly into con-
sideration are opioids, cocaine, amphetamine or amphetamine-like substances, nicotine and
alcohol.

With regard to the treatment of addiction diseases, particular preference is given to those
20   compounds according to the invention of the formula I which themselves do not possess any
psychotropic effect. This can also be observed in a test using rats, which, after having been
administered compounds which can be used in accordance with the invention, reduce their
self administration of psychotropic substances, for example cocaine.

25   According to another aspect of the present invention, the compounds according to the inven-
tion are suitable for treating disturbances whose causes can at least partially be attributed to
an anomalous activity of dopamine D_3 receptors.

According to another aspect of the present invention, the treatment is directed, in particular,
30   toward those disturbances which can be influenced, within the sense of an expedient me-
dicinal treatment, by the binding of preferably exogeneously administered binding partners
(ligands) to dopamine D_3 receptors.

The diseases which can be treated with the compounds according to the invention are fre-
35   quently characterized by progressive development, i.e. the above-described conditions
change over the course of time; as a rule, the severity increases and conditions may possi-
bly merge into each other or other conditions may appear in addition to those which already
exist.

45

The compounds according to the invention can be used to treat a large number of signs, symptoms and/or malfunctions which are connected with the disturbances of the central nervous system and, in particular, the abovementioned conditions. These signs, symptoms and/or malfunctions include, for example, a disturbed relationship to reality, lack of insight

5   and ability to meet customary social norms or the demands made by life, changes in temperament, changes in individual drives, such as hunger, sleep, thirst, etc., and in mood, disturbances in the ability to observe and combine, changes in personality, in particular emotional lability, hallucinations, ego-disturbances, distractedness, ambivalence, autism, depersonalization and false perceptions, delusional ideas, chanting speech, lack of synkinesia,

10   short-step gait, flexed posture of trunk and limbs, tremor, poverty of facial expression, monotonous speech, depressions, apathy, impeded spontaneity and decisiveness, impoverished association ability, anxiety, nervous agitation, stammering, social phobia, panic disturbances, withdrawal symptoms in association with dependency, maniform syndromes, states of excitation and confusion, dysphoria, dyskinetic syndromes and tic disturbances, e.g. Hunt-

15   ington's chorea and Gilles-de-la-Tourette's syndrome, vertigo syndromes, e.g. peripheral positional, rotational and oscillatory vertigo, melancholia, hysteria, hypochondria and the like.

Within the meaning of the invention, a treatment also includes a preventive treatment (prophylaxis), in particular as relapse prophylaxis or phase prophylaxis, as well as the treatment

20   of acute or chronic signs, symptoms and/or malfunctions. The treatment can be orientated symptomatically, for example as the suppression of symptoms. It can be effected over a short period, be orientated over the medium term or can be a long-term treatment, for example within the context of a maintenance therapy.

25   The compounds according to the invention are preferentially suitable for treating diseases of the central nervous system, in particular for treating affective disturbances; neurotic disturbances, stress disturbances and somatoform disturbances and psychoses, and, in particular, for treating schizophrenia and depression. Because of their high selectivity with regard to the D_3 receptor, the compounds I according to the invention are also suitable for treating distur-

30   bances of kidney function, in particular disturbances of kidney function which are caused by diabetes mellitus (see WO 00/67847) and, especially, diabetic nephropathy.

Within the context of the treatment, the use according to the invention of the described compounds involves a method. In this method, an effective quantity of one or more compounds,

35   as a rule formulated in accordance with pharmaceutical and veterinary practice, is administered to the individual to be treated, preferably a mammal, in particular a human being, productive animal or domestic animal. Whether such a treatment is indicated, and in which form it is to take place, depends on the individual case and is subject to medical assessment (diagnosis) which takes into consideration signs, symptoms and/or malfunctions which are pre-

sent, the risks of developing particular signs, symptoms and/or malfunctions, and other factors.

As a rule, the treatment is effected by means of single or repeated daily administration,
5   where appropriate together, or alternating, with other active compounds or active compound-containing preparations such that a daily dose of preferably from about 0.1 to 1000 mg/kg of bodyweight, in the case of oral administration, or of from about 0.1 to 100 mg/kg of bodyweight, in the case of parenteral administration, is supplied to an individual to be treated.

10   The invention also relates to the production of pharmaceutical compositions for treating an individual, preferably a mammal, in particular a human being, productive animal or domestic animal. Thus, the ligands are customarily administered in the form of pharmaceutical compositions which comprise a pharmaceutically acceptable excipient together with at least one ligand according to the invention and, where appropriate, other active compounds. These
15   compositions can, for example, be administered orally, rectally, transdermally, subcutaneously, intravenously, intramuscularly or intranasally.

Examples of suitable pharmaceutical formulations are solid medicinal forms, such as powders, granules, tablets, in particular film tablets, lozenges, sachets, cachets, sugar-coated
20   tablets, capsules, such as hard gelatin capsules and soft gelatin capsules, suppositories or vaginal medicinal forms, semisolid medicinal forms, such as ointments, creams, hydrogels, pastes or plasters, and also liquid medicinal forms, such as solutions, emulsions, in particular oil-in-water emulsions, suspensions, for example lotions, injection preparations and infusion preparations, and eyedrops and eardrops. Implanted release devices can also be used
25   for administering inhibitors according to the invention. In addition, it is also possible to use liposomes or microspheres.
When producing the compositions, inhibitors according to the invention are usually mixed or diluted with an excipient. Excipients can be solid, semisolid or liquid materials which serve as vehicles, carriers or medium for the active compound.
30
Suitable excipients are listed in the specialist medicinal monographs. In addition, the formulations can comprise pharmaceutically acceptable carriers or customary auxiliary substances, such as glidants; wetting agents; emulsifying and suspending agents; preservatives; antioxidants; antiirritants; chelating agents; coating auxiliaries; emulsion stabilizers;
35   film formers; gel formers; odor masking agents; taste corrigents; resin; hydrocolloids; solvents; solubilizers; neutralizing agents; diffusion accelerators; pigments; quaternary ammonium compounds; refatting and overfatting agents; raw materials for ointments, creams or oils; silicone derivatives; spreading auxiliaries; stabilizers; sterilants; suppository bases; tablet auxiliaries, such as binders, fillers, glidants, disintegrants or coatings; propellants; drying
40   agents; opacifiers; thickeners; waxes; plasticizers and white mineral oils. A formulation in

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this regard is based on specialist knowledge as described, for example, in Fiedler, H.P., Lexikon der Hilfsstoffe für Pharmazie, Kosmetik und angrenzende Gebiete [Encyclopedia of auxiliary substances for pharmacy, cosmetics and related fields], 4th edition, Aulendorf: ECV-Editio-Kantor-Verlag, 1996.

5

The following examples serve to explain the invention without limiting it.

The magnetic nuclear resonance spectral properties (NMR) refer to the chemical shifts (δ) expressed in parts per million (ppm). The relative area of the shifts in the ^{1}H NMR spectrum

10   corresponds to the number of hydrogen atoms for a particular functional type in the molecule. The nature of the shift, as regards multiplicity, is indicated as singlet (s), broad singlet (s. br.), doublet (d), broad doublet (d br.), triplet (t), broad triplet (t br.), quartet (q), quintet (quint.) and multiplet (m).

15   Preparation Examples

Example 1: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide

1.1   1-Allyl-4-(5-nitropyridin-2-yl)piperazine

20

2.0 g (12.61 mmol) of 2-chloro-5-nitropyridine were dissolved in 8 ml of dimethylformamide, and 3.49 g (25.23 mmol) of potassium carbonate were added. After that, a solution of 1.75 g (13.88 mmol) of N-allylpiperazine in 2 ml of dimethylformamide was added slowly dropwise to the reaction mixture (exothermic reaction). The reaction mix-

25   ture was then stirred at room temperature for 2 hours. After the solvent had been concentrated down to dryness, the resulting residue was stirred up in 100 ml of heptane. The precipitate which remained was filtered off with suction. The filtrate was concentrated, resulting in 720 mg of the title compound. The precipitate which had been filtered off with suction was treated with 150 ml of water and extracted three times with

30   diethyl ether. The organic phase was washed with a saturated solution of sodium chloride and dried over sodium sulfate. A further 2.24 g of the title compound were isolated after the solvent had been filtered and concentrated down to dryness. The total yield of 1-allyl-4-(5-nitropyridin-2-yl)piperazine was 2.96 g (95% of theory).

35   MS [m+1]: 249.

1.2   6-(4-Allylpiperazin-1-yl)pyridine-3-amine

2.2 g (8.86 mmol) of 1-allyl-4-(5-nitropyridin-2-yl)piperazine from Example 1.1 were

40   dissolved in 150 ml of methanol after which 18 g (79.75 mmol) of tin(II) chloride di-

48

hydrate were added and the mixture was stirred at 70 °C for 4 hours. After the solvent had been evaporated down to dryness, water was added to the residue. The aqueous reaction mixture was made alkaline with dilute sodium hydroxide solution and then extracted with ethyl acetate. The solid which had precipitated out was filtered off. After that, the phases were separated and the aqueous phase was extracted in each case twice with ethyl acetate and dichloromethane. The combined organic phases were dried over sodium sulfate. 1.74 g (90% of theory) of the title compound were obtained after the drying agent had been removed and the solvent had been evaporated down to dryness.

MS [m+1]: 219.

1.3   N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide

1.4 g (7.97 mmol) of 6-(4-allylpiperazin-1-yl)pyridin-3-ylamine from Example 1.2 and 1.74 g (7.97 mmol) of 4-isopropylbenzenesulfonyl chloride were dissolved in 30 ml of tetrahydrofuran at room temperature. 3.3 ml (23.91 mmol) of triethylamine were then added to this mixture. After that, the reaction mixture was stirred overnight at room temperature. After the solvent had been evaporated to dryness, water was added to the residue. The aqueous reaction mixture was made acid with 1N hydrochloric acid and extracted twice with diethyl ether. After that, the aqueous phase was made alkaline (pH 9-10) with a 1N aqueous solution of sodium hydroxide and then extracted twice with diethyl ether. After the combined organic phases had been dried over sodium sulfate, the drying agent had been filtered off and the solvent had been evaporated down to dryness, the resulting residue was chromatographed on silica gel using cyclohexane/ethyl acetate (45:55% to 100% ethyl acetate). The filtrate was evaporated down to dryness. The resulting residue was thoroughly stirred in 10 ml of heptane, filtered off in suction and dried, with 1.93 g (61% of theory) of the title compound being obtained.

^{1}H-NMR (500 MHz, CDCl$_3$): δ [ppm] 7.7 (s, 1H); 7.6 (d, 2H); 7.4 (d, 1H); 7.3 (d, 2H); 6.6 (d, 1H); 6.4 (bs, 1H); 5.9 (m, 1H); 5.2 (m, 2H); 3.5 (m, 4H); 3.1 (m, 2H); 3.0 (m, 1H); 2.5 (m, 4H); 1.2 (d, 6H).

MS [m+1]: 401.

Example 2: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-propylbenzenesulfonamide

373 mg of the title compound were obtained in an analogous manner to that described in Example 1.3 when starting with 4-n-propylbenzenesulfonyl chloride.

49

^{1}H-NMR (500 MHz, CDCl$_3$): δ [ppm] 7.7 (m, 1H); 7.6 (m, 2H); 7.4 (d, 1H); 7.3 (m, 2H); 6.6 (d, 1H); 6.3 (bs, 1H); 5.9 (m, 1H); 5.2 (m, 2H); 3.5 (m, 4H); 3.1 (m, 2H); 2.6 (m, 2H); 2.5 (m, 4H); 1.7 (m, 2H); 0.9 (m, 3H).

5

MS [m+1]: 401.

Example 3: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-butylbenzenesulfonamide

10   405 mg of the title compound were obtained in an analogous manner to that described in Example 1.3 when starting with 4-n-butylbenzenesulfonyl chloride.

^{1}H-NMR (500 MHz, CDCl$_3$): δ [ppm] 7.7 (m, 1H); 7.6 (m, 2H); 7.4 (d, 1H); 7.3 (m, 2H); 6.6 (d, 1H); 6.2 (bs, 1H); 5.9 (m, 1H); 5.2 (m, 2H); 3.5 (m, 4H); 3.0 (m, 2H); 2.7 (m, 15   2H); 2.5 (m, 4H); 1.6 (m, 2H); 1.4 (m, 2H); 0.9 (m, 3H).

MS [m+1]: 415.

Example 4: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-trifluoromethylbenzenesulfonamide
20

500 mg of the title compound were obtained in an analogous manner to that described in Example 1.3 when starting with 4-trifluoromethylbenzenesulfonyl chloride.

^{1}H-NMR (500 MHz, CDCl$_3$): δ [ppm] 7.9 (d, 2H); 7.8 (m, 3H); 7.3 (d, 1H); 6.6 (d, 1H); 25   5.9 (m, 1H); 5.2 (m, 2H); 3.5 (m, 4H); 3.1 (m, 2H); 2.5 (m, 4H).

MS [m+1]: 427.

Example 5: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-ethylbenzenesulfonamide hydrochloride
30

The Example 1.3 was repeated with 4-ethylbenzenesulfonyl chloride being used instead of 4-isopropylbenzenesulfonyl chloride. The resulting reaction product was converted into the hydrochloride with ethereal hydrochloric acid, with 480 mg (please complete) of the title compound being obtained.

35

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 11.5 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 2H); 7.6 (d, 2H); 7.4 (m, 3H); 6.9 (d, 1H); 6.0 (m, 1H); 5.5 (m, 2H); 4.3 (m, 2H); 3.8 (m, 2H); 3.4 (m, 2H); 3.3 (m, 2H); 3.0 (m, 2H); 2.7 (m, 2H); 1.2 (t, 3H).

40   MS [m+1]: 387 (free base).

50

Example 6: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-vinylbenzenesulfonamide hydrochloride

5   Example 1.3 was repeated with 4-vinylbenzenesulfonyl chloride being used instead of
4-isopropylbenzenesulfonyl chloride. The resulting reaction product was converted into
the hydrochloride with ethereal hydrochloric acid, with 300 mg of the title compound
being obtained.

10   ^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] 11.1 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (m,
4H); 7.3 (d, 1H); 6.9 (d, 1H); 6.8 (dd, 1H); 6.0 (m, 2H); 5.5 (m, 3H); 4.3 (m, 2H); 3.8 (m,
2H); 3.4 (m, 2H); 3.2 (m, 2H); 3.0 (m, 2H).

MS [m+1]: 385 (free base).

15   Example 7: 4-Isopropyl-N-(6-piperazin-1-ylpyridin-3-yl)benzenesulfonamide

95 mg (0.1 mmol) of tris-(dibenzylideneacetone)dipalladium(0) and 44 mg (0.1 mmol)
of 1,4-bis-(diphenylphosphino)butane were dissolved in 10 ml of tetrahydrofuran under
an argon atmosphere. A solution composed of 1.1 g (2.75 mmol) of N-[6-(4-
20   allylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide from Example 1.3 l in 3
ml of tetrahydrofuran was then added dropwise to the reaction mixture. After that, a so-
lution of 386 mg (2.5 mmol) of 2-mercaptobenzoic acid in 2 ml of tetrahydrofuran was
added dropwise to the reaction mixture and the mixture was stirred at room tempera-
ture for 90 minutes. A solution of a further 386 mg (2.5 mmol) of 2-mercaptobenzoic ·
25   acid in 2 ml of tetrahydrofuran was then added dropwise to the reaction mixture. The
reaction mixture was stirred overnight at room temperature and, after that, the solvent
was evaporated down to dryness. 150 ml of water were added to the resulting residue,
after which the mixture was made acid with 1N aqueous hydrochloric acid and ex-
tracted three times with diethyl ether. The aqueous phase was then made alkaline, to
30   pH > 11, with a 1N aqueous solution of sodium hydroxide and subsequently extracted
three times with dichloromethane. After that, the aqueous phase was adjusted to pH 8-
9, saturated with an aqueous solution of sodium chloride and, after that, extracted
several times with dichloromethane. 840 mg (82% of theory) of the title compound
were obtained after the combined organic phases had been dried over sodium sulfate
35   and the solvent had been filtered and evaporated down to dryness.

^{1}H-NMR (400 MHz, CDCl$_3$): δ [ppm] 7.7 (d, 1H); 7.6 (d, 2H); 7.4 (dd, 1H); 7.3 (d, 2H);
6.6 (d, 1H); 3.5 (m, 4H); 3.0 (m, 5H); 1.2 (d, 6H).

40   MS [m+1]: 361.

51

Example 8: N-{6-[4-(Cyclohexylmethyl)piperazin-1-yl]pyridin-3-yl}-4-isopropyl-benzenesulfonamide hydrochloride

5   150 mg (0.42 mmol) of 4-isopropyl-N-(6-piperazin-1-yl-pyridin-3-yl)-
       benzenesulfonamide from Example 7 and 51 mg (0.46 mmol) of cyclohexanealdehyde
       were dissolved in 5 ml of dichloromethane and 40 µl (0.62 mmol) of glacial acetic acid
       under a nitrogen atmosphere. 133 mg (0.63 mmol) of sodium trisacetoxyborohydride
       were then added. The mixture was stirred at room temperature for 90 minutes and, af-
10   ter that, the solvent was evaporated down to dryness. The resulting residue was taken
       up in water and this mixture was made to pH > 11 with a 1N aqueous solution of so-
       dium hydroxide. After that, the aqueous reaction mixture was extracted with diethyl
       ether. After the organic phase had been dried over sodium sulfate and the solvent had
       been filtered and evaporated down to dryness, the resulting residue was converted
15   into the hydrochloride with ethereal hydrochloric acid, resulting in 156 mg (76% of the-
       ory) of the title compound.

       ^{1}H-NMR (500 MHz, DMSO-d_6): δ [ppm] 10.4 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (d,
       2H); 7.4 (d, 2H); 7.3 (d, 1H); 6.9 (d, 1H); 4.2 (m, 2H); 3.5 (m, 2H); 3.4 (m, 2H); 3.0 (m,
20   5H); 1.8 (m, 3H); 1.7 (m, 3H); 1.2 (m, 9H); 1.0 (m, 2H).

       MS [m+1]: 457 (free base).

       The compounds of Examples 9 to 12 were prepared in an analogous manner.
25
       Example 9: N-[6-(4-Isobutylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hy-
       drochloride

       ^{1}H-NMR (500 MHz, DMSO-d_6): δ [ppm] 10.4 (bs, 1H); 10.0 (s, 1H); 7.8 (m, 1H); 7.6 (d,
30   2H); 7.5 (d, 2H); 7.4 (m, 1H); 6.9 (d, 1H); 4.2 (d, 2H); 3.5 (d, 2H); 3.4 (m, 2H); 3.0 (m,
       5H); 2.1 (m, 1H); 1.2 (d, 6H); 1.0 (d, 6H).

       MS [m+1]: 417 (free base).

35   Example 10: 4-Isopropyl-N-[6-(4-methylpiperazin-1-yl)pyridin-3-yl]benzenesulfonamide

       ^{1}H-NMR (500 MHz, CDCl$_3$): δ [ppm] 7.7 (d, 1H); 7.6 (d, 2H); 7.4 (dd, 1H); 7.3 (d, 2H);
       6.6 (d, 1H); 3.5 (m, 4H); 3.0 (m, 1H); 2.5 (m, 4H); 2.3 (s, 3H); 1.2 (d, 6H).

40   MS [m+1]: 375.

52

Example 11: N-[6-(4-Ethylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hydrochloride

5 ^{1}H-NMR (500 MHz, DMSO-d$_6$): δ [ppm] 10.4 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.3 (d, 1H); 6.9 (d, 1H); 4.3 (m, 2H); 3.5 (m, 2H); 3.2 (m, 2H); 3.1 (m, 2H); 3.0 (m, 3H); 1.3 (m, 3H); 1.2 (d, 6H).

MS [m+1]: 389 (free base).

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Example 12: N-{6-[4-(Cyclopropylmethyl)piperazin-1-yl]pyridin-3-yl}-4-isopropyl-benzenesulfonamide hydrochloride

15 ^{1}H-NMR (500 MHz, DMSO-d$_6$): δ [ppm] 10.8 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.3 (d, 1H); 6.9 (d, 1H); 4.3 (m, 2H); 3.6 (m, 2H); 3.3 (m, 2H); 3.0 (m, 5H); 1.2 (d, 6H); 1.1 (m, 1H); 0.6 (m, 2H); 0.4 (m, 2H).

MS [m+1]: 415 (free base)

20 Example 13: N-[6-(4-Allyl-3-methylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzene-sulfonamide hydrochloride

13.1 3-Methyl-1-(5-nitropyridin-2-yl)piperazine

25 872 mg (6.31 mmol) of potassium carbonate were added to a solution of 500 mg (3.15 mmol) of 2-chloro-5-nitropyridine in 7 ml of dimethylformamide. After that, a solution of 350 mg (3.32 mmol) of 2-methylpiperazine in 3 ml of dimethylformamide was slowly added dropwise to the reaction mixture while cooling with ice (exothermic reaction). The reaction mixture was stirred for 1 hour while cooling with ice and then stirred over-
30 night at room temperature. After the solvent had been evaporated to dryness, the residue was taken up in water and this mixture was extracted three times with diethyl ether. The combined organic phases were dried over sodium sulfate, filtered and evaporated to dryness, with 3-methyl-1-(5-nitropyridin-2-yl)piperazine (Yield: 650 mg, 89% of theory) being obtained.

35

^{1}H-NMR (500 MHz, CDCl$_3$): δ [ppm] 9.0 (s, 1H); 8.2 (d, 1H); 6.6 (d, 1H), 4.4 (m, 2H); 3.2 (m, 1H); 3.1 (m, 1H); 2.9 (m, 2H); 2.7 (m, 1H); 1.2 (m, 3H).

^{13}C-NMR (125 MHz, CDCl$_3$): 160.4 (C); 146.5 (CH); 134.9 (C); 133.0 (C); 104.5 (CH);
40 52.2 (CH$_2$); 50.6 (CH); 45.7 (CH$_2$); 45.4 (CH$_2$); 19.6 (CH$_3$).

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13.2 1-Allyl-2-methyl-4-(5-nitropyridin-2-yl)piperazine

630 mg (2.72 mmol) of 3-methyl-1-(5-nitropyridin-2-yl)piperazine from Example 13.1 and 267 μl (3.09 mmol) of allyl bromide were dissolved in 10 ml of dimethylformamide. 1.2 ml (8.4 mmol) of triethylamine were then added dropwise to the solution. After the mixture had been stirred at room temperature for 1 hour, a further 65 μl (0.75 mmol) of allyl bromide were added dropwise to the reaction mixture, which was then stirred for a further hour. After that, a further 65 μl (0.75 mmol) of allyl bromide and 0.5 ml (3.6 mmol) of triethylamine were added dropwise. The mixture was then stirred overnight at room temperature. After the solvent had been evaporated down to dryness, the resulting residue was taken up in water and this solution was made alkaline using a 1N aqueous solution of sodium hydroxide. After that, the aqueous reaction mixture was extracted three times with diethyl ether. The combined organic phases were dried over sodium sulfate, filtered and evaporated down to dryness, with 707 mg (90% of theory) of the title compound being obtained.

MS [m+1]: 263.

13.3 6-(4-Allyl-3-methylpiperazin-1-yl)pyridine-3-amine

4.975 g (22.05 mmol) of tin(II) chloride dihydrate were added to a solution of 707 mg (2.45 mmol) of 1-allyl-2-methyl-4-(5-nitropyridin-2-yl)piperazine from Example 13.2 in 50 ml of methanol and the resulting mixture was stirred at 70°C for 90 minutes. After the solvent had been evaporated down to dryness, water was added to the resulting residue and the mixture was made alkaline using a dilute aqueous solution of sodium hydroxide. After that, the aqueous reaction mixture was extracted with ethyl acetate. The solid which had precipitated out was filtered off with suction and the phases were separated. The aqueous phase was extracted with dichloromethane. After that, the combined organic phases were dried over sodium sulfate, filtered and evaporated down to dryness. The resulting title compound was used in the next step without any further purification.

MS [m+1]: 233.

13.4 N-[6-(4-Allyl-3-methylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hydrochloride

305 mg (1.31 mmol) of 6-(4-allyl-3-methylpiperazin-1-yl)pyridin-3-ylamine from Example 13.3 and 301 mg (1.38 mmol) of 4-isopropylbenzenesulfonyl chloride were dis-

solved in 10 ml of tetrahydrofuran at room temperature, after which 0.55 ml (3.94 mmol) of triethylamine was added dropwise. After that, the reaction mixture was stirred overnight at room temperature. After the solvent had been evaporated down to dryness, the resulting residue was treated with water and the mixture was made acid with
5   1N hydrochloric acid and extracted twice with diethylether. The aqueous phase was made alkaline, to pH 9-10, using a 1N aqueous solution of sodium hydroxide and then extracted twice with diethyl ether. After the combined organic phases had been dried over sodium sulfate and the solvent had been filtered and evaporated down to dryness, the resulting residue was purified by column chromatography (cyclohex-
10   ane/ethylacetate from 50:50 to 20:80). After that, the filtrate was evaporated down to dryness. The resulting residue was converted into the hydrochloride using ethereal hydrochloric acid, with 417 mg (74% of theory) of the title compound being obtained.

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 11.3 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (d,
15   2H); 7.4 (d, 2H); 7.3 (d, 1H); 6.9 (d,1 H); 6.0 (m, 1H); 5.5 (m, 2H); 4.3 (m, 1H); 4.0 (m, 1H); 3.7 (m, 1H); 3.4 (m, 1H); 3.2 (m, 3H); 3.0 (m, 3H); 1.4 (d, 3H); 1.2 (d, 6H).

MS [m+1]: 415 (free base).

20   Example 13a: N-{6-[4-Allyl-(3S)-methylpiperazin-1-yl]pyridin-3-yl}-4-isopropylbenzene-sulfonamide (S enantiomer as free base)

The preparation was effected in analogy with the preparation of the racemic compound, with enantiomerically pure (2S)-methylpiperazine being used in step 13.1 in-
25   stead of racemic 2-methylpiperazine.

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 11.3 (bs, 1H); 10.0 (s, 1H); 7.8 (s, 1H); 7.6 (d, 2H); 7.4 (d, 1H); 7.3 (d, 1H); 6.9 (d, 1H); 6.0 (m, 1H); 5.5 (m, 2H); 4.3 (m, 2H); 4.0 (m, 1H); 3.7 (m, 1H); 3.4 (m, 1H); 3.2 (m, 2H); 3.1 (m, 1H); 3.0 (m, 2H).1.4 (d, 3H); 1.2 (d,
30   6H).

MS [m+1]: 415 (free base)

Example 14: 4-Isopropyl-N-[6-(3-methyl-4-propylpiperazin-1-yl)pyridin-3-
35   yl]benzenesulfonamide hydrochloride

100 mg (0.24 mmol) of N-[6-(4-allyl-3-methylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hydrochloride from Example 13.4 were dissolved in 10 ml of ethyl acetate, after which 10 mg of palladium on active charcoal (10%) were added
40   and the mixture was stirred overnight at room temperature under a hydrogen atmos-

55

phere. After that, the catalyst was filtered off and the filtrate was evaporated down to dryness. After 1 ml of dichloromethane had been added to the resulting residue, diethyl ether was slowly added dropwise until the solution became cloudy. The reaction mixture was stirred for 30 minutes and the precipitate which had formed was filtered off with suction. The filtrate was evaporated down to dryness, after which the residue was dissolved in a 1:1 mixture of dichloromethane and diethyl ether and converted into the hydrochloride by adding ethereal hydrochloric acid. 71 mg (63% of theory) of the title compound were obtained.

^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] 10.9 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.3 (d, 1H); 6.9 (d,1 H); 4.2 (m, 2H); 3.6 (m, 1H); 3.4-3.0 (m, 7H); 1.7 (m, 2H); 1.4 (d, 3H); 1.2 (d, 6H); 0.9 (m, 3H).

MS [m+1]: 417 (free base).

Example 14a: 4-Isopropyl-N-{6-[(3S)-methyl-4-propylpiperazin-1-yl]pyridin-3-yl}benzenesulfonamide as free base (S enantiomer)

The preparation was effected in analogy with the preparation of the racemic compound, with enantiomerically pure (2S)-methylpiperazine being used instead of racemic 2-methylpiperazine.

^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] 9.7 (s, 1H); 7.7 (s, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.2 (d, 1H); 6.7 (d,1 H); 3.8 (m, 2H); 2.9 (m, 2H); 2.8 (m, 1H); 2.6 (m, 2H); 2.3 (m, 1H), 2.1 (m, 2H); 1.4 (m, 2H); 1.2 (d, 6H); 1.0 (m, 3H); 0.8 (m, 3H).

MS [m+1]: 417 (free base)

Example 15: N-[5-(4-Allylpiperazin-1-yl)pyridin-2-yl]-4-isopropylbenzenesulfonamide hydrochloride

15.1   1-Allyl-4-(6-nitropyridin-3-yl)piperazine

315 mg (2.5 mmol) of N-allylpiperazine were dissolved in 5 ml of toluene under an argon atmosphere. 93 mg (0.1 mmol) of tris-(dibenzylideneacetone)-dipalladium(0) (Pd$_2$dba$_3$), 126 mg (0.2 mmol) of 2,2'-bis-(diphenylphosphino)-1,1'-binaphthyl (BINAP), 1.14 g (3.5 mmol) of cesium carbonate and 515 mg (2.54 mmol) of 5-bromo-2-nitropyridine were then added and the mixture was stirred at 120°C, in a microwave oven, for 4 hours. After the reaction mixture had cooled down to room temperature, a saturated aqueous solution of ammonium chloride was added. After that, the aqueous

reaction mixture was extracted three times with in each case 50 ml of ethyl acetate. After the organic phase had been dried over sodium sulfate, the drying agent had been filtered off and the solvent had been evaporated down to dryness, the residue was chromatographed through silica gel using ethyl acetate/methanol (4:1), with 304 mg (46% of theory) of the title compound being obtained.

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^{1}H-NMR (400 MHz, CDCl$_3$): δ [ppm] 8.2 (m, 2H); 7.2 (dd, 1H); 5.9 (m, 1H); 5.3 (m, 2H); 3.5 (m, 4H); 3.1 (m, 2H); 2.6 (m, 4H).

10   MS [m+1]: 249

15.2   5-(4-Allylpiperazin-1-yl)pyridine-2-amine

300 mg (1.21 mmol) of 1-allyl-4-(6-nitropyridin-3-yl)piperazine from Example 15.1 were

15   dissolved in 20 ml of methanol, after which 2.18 g (9.67 mmol) of tin(II) chloride dihydrate were added and the mixture was stirred at 70°C for 2 hours. After the solvent had been evaporated down to dryness, the resulting residue was treated with water and this mixture was made alkaline using a dilute aqueous solution of sodium hydroxide and extracted with ethyl acetate. The solid which had precipitated out was filtered

20   off with suction. The phases were then separated and the aqueous phase was extracted three times with ethyl acetate. The combined organic phases were dried over sodium sulfate, filtered and evaporated down to dryness, with 183 mg (69% of theory) of the title compound being obtained.

25   MS [m+1]: 219.

15.3   N-[5-(4-Allylpiperazin-1-yl)pyridin-2-yl]-4-isopropylbenzenesulfonamide hydrochloride

520 mg (2.38 mmol) of 5-(4-allylpiperazin-1-yl)pyridin-2-ylamine and 495 mg (2.26

30   mmol) of 4-isopropylbenzenesulfonyl chloride were dissolved in 5 ml of tetrahydrofuran at room temperature, after which 1.0 ml (7.15 mmol) of triethylamine was added dropwise and the mixture was stirred at 40-50°C for 6 hours. After the solvent had been evaporated down to dryness, the resulting residue was treated with water and this mixture was made acid using 1N aqueous hydrochloric acid and extracted twice with di-

35   ethyl ether. The aqueous phase was made alkaline, to pH 9-10, using a 1N aqueous solution of sodium hydroxide and then extracted twice with ethyl acetate. After the combined organic phases had been dried over sodium sulfate, the drying agent had been filtered off and the solvent had been evaporated down to dryness, the resulting residue was chromatographed on silica gel using ethyl acetate. After the solvent had

40   been removed, the resulting residue was brought into solution using a little diethyl

ether in dichloromethane and then converted into the hydrochloride using ethereal hydrochloric acid. 415 mg (44% of theory) of the title compound were obtained.

5
^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 11.6 (bs, 1H); 7.9 (d, 1H); 7.8 (d, 2H); 7.5 (dd, 1H); 7.4 (d, 2H); 7.1 (d, 1H); 6.0 (m, 1H); 5.5 (m, 2H); 3.7 (m, 4H); 3.4 (m, 2H); 3.1 (m, 4H); 3.0 (m, 1H); 1.2 (d, 6H).

^{13}C-NMR (100 MHz, DMSO-d$_6$): δ [ppm] 153.3 (C); 144.5 (C); 141.6 (C); 138.4 (C); 134.3 (CH); 127.3 (CH); 127.0 (CH); 126.8 (CH); 124.8 (CH$_2$); 113.8 (CH); 57.3 (CH$_2$);
10
49.6 (CH$_2$); 45.2 (CH$_2$); 33.3 (CH); 23.4 (CH$_3$).

MS [m+1]: 401.

Example 16: N-[2-(4-Allylpiperazin-1-yl)pyrimidin-5-yl]-4-isopropylbenzenesulfonamide
15

16.1 2-(4-Allylpiperazin-1-yl)-5-nitropyrimidine

114 mg (2.38 mmol) of 50% sodium hydride were added, under a nitrogen atmosphere and while cooling with ice, to a solution of 273 mg (2.17 mmol) of N-allylpiperazine in 5
20
ml of dimethylformamide. After 30 minutes, a solution of 440 mg (2.17 mmol) of 2-(methylsulfone)-5-nitropyrimidine in 5 ml of dimethylformamide was added dropwise to the reaction mixture. After 10 minutes, 70 ml of water were added and the reaction mixture was extracted twice with in each case 50 ml of ethyl acetate. After the combined organic phases had been dried over sodium sulfate, the drying agent had been
25
filtered off and the solvent had been evaporated to dryness, 535 mg (99% of theory) of the title compound were obtained.

^{1}H-NMR (400 MHz, CDCl$_3$): δ [ppm] 9.0 (s, 2H); 5.8 (m, 1H); 5.2 (m, 2H); 4.0 (m, 4H); 3.1 (m, 2H); 2.5 (m, 4H).
30
MS [m+1]: 250.

16.2 2-(4-Allylpiperazin-1-yl)pyrimidine-5-amine

35
3.84 g (17.0 mmol) of tin(II) chloride dihydrate were added to a solution of 530 mg (2.13 mmol) of 2-(4-allylpiperazin-1-yl)-5-nitropyrimidine from Example 16.1 in 20 ml of methanol and, after that, the reaction mixture was heated at reflux for 1 hour. After the solvent had been evaporated to dryness, the residue was treated with saturated aqueous sodium chloride solution and then made alkaline using dilute aqueous sodium hy-
40
droxide solution. After that, the aqueous reaction mixture was extracted with ethyl ace-

tate. The solid which had precipitated out was filtered off with suction. The phases were then separated and the aqueous phase was extracted in each case twice with ethyl acetate and dichloromethane. After the combined organic phases had been dried over sodium sulfate, the drying agent had been filtered off and the solvent had been evaporated down to dryness, 220 mg (46% of theory) of the title compound were obtained.

16.3 N-[2-(4-Allylpiperazin-1-yl)pyrimidin-5-yl]-4-isopropylbenzenesulfonamide

216 mg (0.98 mmol) of 2-(4-Allylpiperazin-1-yl)pyrimidin-5-ylamine from Example 16.2 and 215 mg (0.98 mmol) of 4-isopropylbenzenesulfonyl chloride were dissolved in 20 ml of tetrahydrofuran at room temperature, after which 0.4 ml (3.0 mmol) of triethylamine was added dropwise and the mixture was stirred at room temperature overnight. After the solvent had been evaporated down to dryness, water was added to the resulting residue. The aqueous reaction mixture was made acid using 1N aqueous hydrochloric acid and extracted twice with diethyl ether. The aqueous phase was made alkaline to pH 9-10, using a 1N solution of sodium hydroxide and then extracted three times with diethyl ether. The combined organic phases were dried over sodium sulfate. The residue which was obtained after filtering off the drying agent and evaporating the solvent down to dryness was thoroughly stirred with a mixture composed of heptane and diethyl ether, filtered off with suction and dried, with 71 mg (18% of theory) of the title compound being obtained.

^{1}H-NMR (500 MHz, CDCl$_3$): δ [ppm] 8.0 (s, 2H); 7.7 (d, 2H); 7.3 (d, 2H); 6.2 (bs, 1H); 5.9 (m, 1H); 5.2 (m, 2H); 3.8 (m, 4H); 3.1 (m, 2H); 3.0 (m, 1H); 2.5 (m, 4H); 1.3 (d, 6H).

MS [m+1]: 402.

Example 17: 4-Isopropyl-N-[2-(4-propylpiperazin-1-yl)pyrimidin-5-yl]benzenesulfonamide hydrochloride

70 mg (0.17 mmol) of N-[2-(4-allylpiperazin-1-yl)pyrimidin-5-yl]-4-isopropylbenzenesulfonamide from Example 16.3 were dissolved in 30 ml of ethyl acetate, after which 10 mg of palladium on active charcoal (10%) were added and the mixture was stirred at room temperature for 2 hours under a hydrogen atmosphere. The catalyst was then filtered off and the filtrate was concentrated by evaporation. The residue was brought into solution using 25 ml of diethyl ether and converted into the hydrochloride with ethereal hydrochloric acid, resulting in 58 mg (76% of theory) of the title compound being obtained.

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 11.0 (bs, 1H); 10.0 (s, 1H); 8.1 (s, 2H); 7.7 (d, 2H); 7.5 (d, 2H); 4.6 (m, 2H); 3.5 (m, 2H); 3.4 (m, 2H); 3.0 (m, 5H); 1.7 (m, 2H); 1.3 (d, 6H); 0.9 m, 3H).

5   MS [m+1]: 404 (free base).

Example 18: N-[6-(4-Allylpiperazin-1-yl)pyrimidin-4-yl]-4-isopropylbenzenesulfonamide

18.1 N-(6-Chloropyrimidin-4-yl)-4-isopropylbenzenesulfonamide

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996 mg (5.0 mmol) of isopropylbenzenesulfonamide were dissolved in 20 ml of di-methyl sulfoxide, after which 288 mg (6.0 mmol) of 50% sodium hydride were added and the mixture was stirred at room temperature for 30 minutes. 819 mg (5.5 mmol) of 4,6-dichloropyrimidine were then added and the reaction mixture was stirred overnight at room temperature. Subsequently, the mixture was heated at 90°C for 3 hours and, after that, stirred at 120°C, in a microwave oven, for 30 minutes. After the reaction mix-ture had cooled down to room temperature, it was diluted with 150 ml of water, neutral-ized with citric acid and extracted three times with diethyl ether. The residue, which was obtained after drying with sodium sulfate and after removing the solvent, was dis-solved in 100 ml of diethyl ether and extracted with an aqueous solution of sodium hy-drogen carbonate. The aqueous phase was acidified and extracted with diethyl ether. The organic phase was dried, filtered and evaporated down to dryness, with 440 mg (28% of theory) of the title compound being obtained.

25   MS [m+1]: 312.

18.2 N-[6-(4-Allylpiperazin-1-yl)pyrimidin-4-yl]-4-isopropylbenzenesulfonamide

430 mg (1.38 mmol) of N-(6-chloropyrimidin-4-yl)-4-isopropylbenzenesulfonamide from Example 18.1 were dissolved in 3 ml of dimethyl sulfoxide, after which 1.74 g (13.79 mmol) of N-allylpiperazine were added and the mixture was stirred overnight. Subse-quently, the reaction mixture was stirred at 100°C, in a microwave oven, for 45 min-utes. After the reaction mixture had cooled down to room temperature, it was diluted with 50 ml of water. After that, the aqueous reaction mixture was extracted with 50 ml of ethyl acetate and the precipitate was filtered off with suction, with 190 mg (34% of theory) of the title compound being obtained.

^{1}H-NMR (400 MHz, CDCl$_3$): δ [ppm] 8.4 (s, 1H); 7.8 (d, 2H); 7.3 (d, 2H); 6.1 (s, 1H); 5.9 (m, 1H); 5.2 (m, 2H); 3.6 (m, 4H); 3.0 (m, 3H); 2.5 (m, 4H); 1.3 (d, 6H).

40

MS [m+1]: 402.

Example 19: N-[2-(4-Allylpiperazin-1-yl)pyridin-5-yl]-4-bromobenzenesulfonamide hydrochloride

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The preparation was effected in analogy with Example 1.3, with 4-bromobenzenesulfonyl chloride being used instead of 4-isopropylbenzenesulfonyl chloride. The reaction product which was obtained was converted into the hydrochloride using ethereal hydrochloric acid, resulting in 398 mg of the title compound.

10

MS [m+1]: 436/438

Example 20: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-cyclopropylbenzenesulfonamide

15   398 mg (0.84 mmol) of N-[6-(4-allylpiperazin-1-yl)pyridin-3-yl]-4-bromobenzene-sulfonamide from Example 19, 101 mg (1.18 mmol) of cylcopropylboronic acid, 676 mg (3.19 mmol) of K_3PO_4 and 26 mg (0.09 mmol) of tricyclohexylphosphine were dissolved in 4 ml of toluene and 0.2 ml of water under a nitrogen atmosphere. 10 mg (0.04 mmol) of palladium(II) acetate were then added and the mixture was stirred at

20   100°C, in a microwave oven, for one hour. After the solvent had been evaporated down to dryness, the resulting residue was treated with water and the mixture was then extracted with ethyl acetate. Because the phases only separated poorly, the finely divided solid was filtered off. The aqueous phase was extracted twice with ethyl acetate. After the combined organic phases had been dried over sodium sulfate and the

25   solvent had been filtered and evaporated down to dryness, the resulting residue was purified by column chromatography.

MS [m+1]: 399

^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm]   11.1 (bs, 1H); 9.9 (s, 1H); 7.8 (s, 1H); 7.6 (d,

30   2H); 7.3 (dd, 1H); 7.2 (d, 2H); 6.9 (d, 1H); 6.0 (m, 1H); 5.5 (d, 2H); 4.3 (m, 2H); 3.8 (m, 2H); 3.4 (m, 2H); 3.2 (m, 2H); 3.0 (m, 2H); 2.0 (m, 1H); 1.0 (m, 2H); 0.8 (m, 2H).

The compounds of the following examples 21 to 40 were prepared in analogous manner:

35   Example 21: 4-Isopropyl-N-[2-(4-propylpiperazin-1-yl)pyridin-3-yl]-benzenesulfonamide hydrochloride

MS [m+1]: 403 (free base).

61

Example 22: 4-Isopropyl-N-[2-(3,5-dimethyl-4-propylpiperazin-1-yl)pyridin-3-yl]benzene-
sulfonamide trifluoroacetate

MS [m+1]: 431 (free base).

5

Example 23: N-[2-(4-Allyl-3-methylpiperazin-1-yl)pyridin-3-yl]-4-trifluoromethyl-
benzenesulfonamide hydrochloride

MS [m+1]: 441 (free base).

10

Example 24: *N*-[6-(4-Allyl-3,5-dimethylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzene-
sulfonamide hydrochloride

MS [m+1]: 429 (free base)

15

Example 25: *N*-[6-(4-Allyl-3,5-dimethylpiperazin-1-yl)pyridin-3-yl]-4-trifluoromethyl-
benzenesulfonamide hydrochloride

MS [m+1]: 455 (free base)

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Example 26: *N*-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-trifluoromethylbenzenesulfonamide

MS [m+1]: 427

25   Example 27: 4-Bromo-*N*-[6-(4-propylpiperazin-1yl)pyridin-3-yl]-benzenesulfonamide

MS [m+1]: 439/441

Example 28: 4-Chloro-*N*-[6-(4-propylpiperazin-1yl)pyridin-3-yl]-benzenesulfonamide

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MS [m+1]: 395

Example 29: 4-Isopropyl-*N*-[6-(5-propyl-2,5-diazabicyclo[2.2.1]hept-2-yl)pyridin-3-yl]-
benzenesulfonamide hydrochloride

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MS [m+1]: 415 (free base)

Example 30: *N*-[6-(5-Allyl-2,5-diazabicyclo[2.2.1]hept-2-yl)pyridin-3-yl]-4-isopropylbenzene-
sulfonamide hydrochloride

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MS [m+1]: 413 (free base)

Example 31: *N*-[6-(4-Propylpiperazin-1-yl)pyridin-3-yl]-4-vinylbenzenesulfonamide hydrochloride

MS [m+1]: 387 (free base)

Example 32: *N*-{6-[4-(3-Fluoropropyl)piperazin-1-yl]pyridin-3-yl}-4-isopropylbenzene-sulfonamide hydrochloride

MS [m+1]: 421 (free base)

Example 33: 4-Isopropyl-*N*-[6-(4-prop-2-yn-1-ylpiperazin-1-yl)pyridin-3-yl]-benzene-sulfonamide hydrochloride

MS [m+1]: 399 (free base)

Example 34: 4-Ethyl-*N*-[6-(4-propylpiperazin-1-yl)pyridin-3-yl]-benzenesulfonamide hydro-chloride

MS [m+1]: 389 (free base)

Example 35: *N*-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-chlorobenzenesulfonamide hydrochloride

MS [m+1]: 393 (free base)

Example 36: 4-Isopropyl-*N*-(4-methyl-6-piperazin-1-ylpyridin-3-yl)-benzenesulfonamide hy-drochloride

MS [m+1]: 375 (free base)

Example 37: *N*-[6-(4-Allylpiperazin-1-yl)-4-methylpyridin-3-yl]-4-isopropylbenzene-sulfonamide hydrochloride

MS [m+1]: 415 (free base)

Example 38: 4-Isopropyl-*N*-[4-methyl-6-(4-propylpiperazin-1-yl)pyridin-3-yl]-benzene-sulfonamide hydrochloride

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MS [m+1]: 417 (free base)

Example 39: *N*-[4-Methyl-6-(4-propylpiperazin-1-yl)pyridin-3-yl]-4-vinylbenzenesulfonamide hydrochloride

MS [m+1]: 401 (free base)

Example 40: *N*-[6-(4-Butylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hydrochloride

MS [m+1]: 417 (free base)

Example 41: *N*-{6-[(3*S*)-4-Ethyl-3-methylpiperazin-1-yl]pyridin-3-yl}-4-isopropylbenzenesulfonamide hydrochloride

MS [m+1]: 403 (free base)

Example 42: N-[2-(4-Allylpiperazin-1-yl)pyridin-5-yl]-4-(N-pyrrolidinyl)benzenesulfonamide fumarate

Reaction of 0.300 g of 6-(4-allylpiperazin-1-yl)-2-methylpyridin-3-amine (1.29 mmol) and 0.282 g of 4-isopropylbenzene-1-sulfonyl chloride (1.29 mmol) in 10 ml of a mixture of pyridine and dichloromethane (1:2) yielded 0.465 g (87 %) of the title compound as a white solid. The title compound was onverted into the fumarate salt in methanol by addition of fumaric acid.

MS [m+1]: 415

^{1}H-NMR (400 MHz, CH$_3$OD): δ [ppm]: 7.6 (d, 2H), 7.5 (d, 2H), 7.3 (m, 1H), 7.2 (m, 1H), 7.1 (d, 1H), 6.5 (d, 1H), 5.9 (m, 1H), 5.4 (m, 2H), 3.5 (m, 5H), 3.0 (m, 4H), 2.8 (m, 2H), 1.9 (s, 3H), 1.2 (m, 6H).

Example 43: 4-Isopropyl-[N-[2-(4-allylpiperazin-1-yl)-6-methylpyridin-5-yl]-4-(N-pyrrolidinyl)benzenesulfonamide, Fumarate

Reaction of 0.300 g of 6-(4-allylpiperazin-1-yl)-2-methylpyridin-3-amine (1.29 mmol) and 0.282 g of 4-isopropylbenzene-1-sulfonyl chloride (1.29 mmol) in 10 ml of a mixture of pyridine/dichloromethane (1:2) yielded 0.465 g (87 %) of the title compound as a white solid. The title compound was onverted into the fumarate salt in methanol by addition of fumaric acid.

64

MS [m+1]: 415

^{1}H-NMR (400 MHz, MeOD): δ [ppm]　7.6 (d, 2H), 7.5 (d, 2H), 7.3 (m, 1H), 7.2 (m, 1H),
7.1 (d, 1H), 6.5 (d, 1H), 5.9 (m, 1H), 5.4 (m, 2H), 3.5 (m, 5H), 3.0 (m, 4H), 2.8 (m, 2H), 1.9
(s, 3H), 1.2 (m, 6H).

Example 44: 4-*tert*-Butyl-[N-[2-(4-allylpiperazin-1-yl)-6-methylpyridin-5-yl]-
benzenesulfonamide, fumarate

Reaction of 0.300 g of 6-(4-allylpiperazin-1-yl)-2-methylpyridin-3-amine (1.29 mmol) and
0.300 g of 4-tert-butylbenzene-1-sulfonyl chloride (1.29 mmol) in 10 ml of a mixture of pyri-
dine/dichloromethane (1:2) yielded 0.525 g (95 %) of the title compound as a white solid.
The title compound was onverted into the fumarate salt in methanol by addition of fumaric
acid.

MS [m+1]: 429

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm]　9.3 (s, 2H), 8.6 (d, 2H), 7.8 (m, 1H), 7.4 (m, 2H),
7.0 (d, 1H), 6.6 (d, 1H), 5.8 (m, 1H), 5.2 (m, 2H), 3.4 (m, 4H), 2.9 (m, 2H), 2.4 (m, 4H), 1.9
(s, 3H), 1.3 (s, 9H).

Example 45: 4-tert-pentyl-[N-[2-(4-Allylpiperazin-1-yl)-6-methylpyridin-5-yl]-
benzenesulfonamide, Fumarate

Reaction of 0.300 g of 6-(4-allylpiperazin-1-yl)-2-methylpyridin-3-amine (1.29 mmol) and
0.318 g of 4-tert-pentylbenzene-1-sulfonyl chloride (1.29 mmol) in 10 mL pyridine-
dichloromethane (1:2) yielded 0.564 g (99 %) of the title compound as a white solid. The title
compound was onverted into the fumarate salt in methanol by addition of fumaric acid.

MS [m+1]: 443
^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm]　9.3 (s, 2H), 8.6 (d, 2H), 7.8 (m, 1H), 7.4 (m, 2H),
7.0 (d, 1H), 6.5 (d, 1H), 5.8 (m, 1H), 5.2 (m, 2H), 3.4 (m, 4H), 3.0 (m, 2H), 2.4 (m, 4H), 1.9
(s, 3H), 1.6 (m, 2H), 1.2 (s, 6H), 0.6 (t, 3H).

The compounds of Examples 46 to　were prepared in analogous manner:

Example 46: 4-Ethyl-N-[6-((S)-3-methyl-4-propyl-piperazin-1-yl)-pyridin-3-yl]-
benzenesulfonamide, hydrochloride

65

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 10.9 (bs, 1H); 10.0 (s, 1H); 7.8 (m, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.3 (dd, 1H); 6.9 (d, 1H); 4.3 (m, 2H); 3.5-2.9 (m, 7H); 2.7 (m, 2H); 1.7 (m, 2H); 1.4 (m, 2H); 1.2 (m, 4H); 0.9 (t, 3H).

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MS [m+1]: 403

Example 47: N-[6-((S)-3-methyl-4-propyl-piperazin-1-yl)-pyridin-3-yl]-4-vinyl-benzenesulfonamide, hydrochloride

10

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 10.4 (bs, 1H); 10.0 (s, 1H); 7.8 (s, 1H); 7.7 (m, 4H); 7.3 (d, 1H); 6.9 (d, 1H); 6.8 (dd, 1H); 6.0 (d, 1H); 5.4 (d, 1H); 4.3 (m, 2H); 3.5 (m, 1H); 3.3-2.9 (m, 6H); 1.7 (m, 2H); 1.4 (m, 2H); 1.2 (m, 1H); 0.9 (t, 3H).

15   MS [m+1]: 401

Example 48: N-[6-((S)-4-Allyl-3-methyl-piperazin-1-yl)-2-methoxy-pyridin-3-yl]-4-isopropyl-benzenesulfonamide, hydrochloride

20   ^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 11.1 (bs, 1H); 9.2 (s, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.3 (m, 1H); 6.4 (m, 1H); 6.0 (m, 1H); 5.5 (m, 2H); 4.3 (m, 2H); 4.0 (m, 1H); 3.7 (m, 2H); 3.4-3.2 (m, 5H); 3.1 (m, 1H); 3.0 (m, 2H); 1.4 (m, 2H); 1.2 (m, 7H).

MS [m+1]: 445

25

Example 49: 4-Isopropyl-N-[2-methoxy-6-((S)-3-methyl-4-propyl-piperazin-1-yl)-pyridin-3-yl]-benzenesulfonamide, hydrochloride

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 10.8 (bs, 1H); 9.3 (s, 1H); 7.6 (d, 2H); 7.4 (d, 2H);
30   7.3 (m, 1H); 6.4 (m, 1H); 4.2 (m, 2H); 3.5-3.2 (m, 8H); 3.1 (m, 1H); 3.0 (m, 2H); 1.7 (m, 2H); 1.4 (m, 2H); 1.2 (m, 7H); 0.9 (t, 3H).

MS [m+1]: 447

35   Example 50: N-[6-((S)-4-Allyl-3-ethyl-piperazin-1-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide, hydrochloride

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 11.2 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.3 (m, 1H); 6.9 (d, 1H); 6.0 (m, 1H); 5.5 (m 2H); 4.2 (m, 2H); 4.0 (m, 2H); 3.4-
40   3.0 (m, 6H); 1.7 (m, 2H); 1.2 (d, 6H); 1.0 (t, 3H).

66

MS [m+1]: 429

Example 51: N-[6-((S)-3-Ethyl-4-propyl-piperazin-1-yl)-pyridin-3-yl]-4-isopropyl-
5   benzenesulfonamide, hydrochloride

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 11.2 (bs, 1H); 10.2 (s, 1H); 7.8 (d, 1H); 7.7 (d, 2H); 7.4 (m, 3H); 7.0 (d, 1H); 4.2 (m, 2H); 3.6-3.0 (m, 8H); 2.0 (m, 1H); 1.7 (m, 3H); 1.2 (d, 6H); 1.0 (m, 6H).

10

MS [m+1]: 431

Example 52: 4-Isopropyl-N-(2-piperazin-1-yl-pyrimidin-5-yl)-benzenesulfonamide

15   ^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 8.0 (s, 2H); 7.6 (d, 2H); 7.4 (d, 2H); 3.6 (m, 4H); 3.0 (m, 1H); 2.7 (m, 4H); 1.2 (d, 6H).

MS [m+1]: 362

20   Example 53: N-[2-(4-Ethyl-piperazin-1-yl)-pyrimidin-5-yl]-4-isopropyl-benzenesulfonamide, hydrochloride

^{1}H-NMR (400 MHz, D$_2$O): δ [ppm] 7.7 (s, 2H); 7.3 (d, 2H); 7.1 (d, 2H); 4.3 (m, 2H); 3.3 (m, 2H); 3.0 (m, 4H); 2.7 (m, 3H); 1.0 (t, 3H); 0.9 (d, 6H).

25

MS [m+1]: 390

Example 54: N-[2-((S)-4-Ethyl-3-methyl-piperazin-1-yl)-pyrimidin-5-yl]-4-isopropyl-
benzenesulfonamide, hydrochloride

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^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 10.7 (bs, 1H); 10.0 (s, 1H); 8.1 (m, 2H); 7.6 (d, 2H); 7.4 (d, 2H); 4.6 (m, 2H); 3.4 (m, 4H); 3.2 (m, 1H); 3.0 (m, 3H); 1.4 (m, 2H); 1.2 (m, 10H).

MS [m+1]: 404

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Example 55: N-[2-((S)-4-Allyl-3-methyl-piperazin-1-yl)-pyrimidin-5-yl]-4-isopropyl-benzene-
sulfonamide, hydrochloride

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 11.0 (bs, 1H); 10.0 (s, 1H); 8.1 (s, 2H); 7.6 (d, 2H); 7.4 (d, 2H); 6.0 (m, 1H); 5.5 (m, 2H); 4.6 (m, 2H); 4.0 (m, 2H); 3.7 (m, 2H); 3.3 (m, 3H); 3.0 (m, 1H); 1.4 (m, 2H); 1.2 (m, 7H).

5 MS [m+1]: 416

Example 56: 4-Isopropyl-N-[2-((S)-3-methyl-4-propyl-piperazin-1-yl)-pyrimidin-5-yl]-benzenesulfonamide, hydrochloride

10 ^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 10.6 (bs, 1H); 10.0 (s, 1H); 8.1 (m, 2H); 7.6 (d, 2H); 7.4 (d, 2H); 4.5 (m, 2H); 3.5 (m, 2H); 3.3 (m, 3H); 3.0 (m, 3H); 1.7 (m, 2H); 1.4 (m, 2H); 1.2 (m, 7H); 0.9 (t, 3H).

MS [m+1]: 418

15

Example 57: 4-Ethyl-N-[2-((S)-3-methyl-4-propyl-piperazin-1-yl)-pyrimidin-5-yl]-benzenesulfonamide, hydrochloride

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 10.8 (bs, 1H); 10.0 (s, 1H); 8.1 (m, 2H); 7.6 (d, 2H);
20 7.4 (d, 2H); 4.5 (m, 2H); 3.5 (m, 2H); 3.3 (m, 3H); 3.0 (m, 2H); 2.7 (m, 2H); 1.7 (m, 2H); 1.4 (m, 2H); 1.2 (m, 4H); 0.9 (t, 3H).

MS [m+1]: 404

25 Example 58: N-[2-((S)-3-Methyl-4-propyl-piperazin-1-yl)-pyrimidin-5-yl]-4-vinyl-benzenesulfonamide, hydrochloride

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] 10.7 (bs, 1H); 10.0 (s, 1H); 8.1 (d, 2H); 7.7 (m, 4H); 6.8 (dd, 1H); 6.0 (d, 1H); 5.5 (d, 1H); 4.5 (m, 2H); 3.5 (m, 2H); 3.3 (m, 3H); 3.0 (m, 2H); 1.7
30 (m, 2H); 1.4 (m, 2H); 1.2 (m, 1H); 0.9 (t, 3H).

MS [m+1]: 402

Example 59: 4-Isopropyl-benzenesulfonic acid 6-(4-allyl-piperazin-1-yl)-pyridin-3-yl ester
35

59.1 4-Isopropyl-benzenesulfonic acid 6-chloro-pyridin-3-yl ester

A reaction flask containing 500 mg of 6-chloropyridin-3-ol (3.86 mmol) and 844 mg of 4-isopropyl-benzenesulfonylchloride (0.20 mmol) in dry tetrahydrofurane (10 ml) was flushed
40 with N$_2$. 1.6 ml of triethylamine were added and the reaction mixture was stirred at room

68

temperature for 2 h. Thereby 4-isopropyl-benzenesulfonic acid 6-chloro-pyridin-3-yl ester ester was obtained in 98 % yield.

MS [m+1]: 312

5 ^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm]   8.1 (d, 1H); 7.8 (d, 2H); 7.6 (m, 4H); 3.0 (m, 1H); 1.2 (d, 6H).

59.2 4-Isopropyl-benzenesulfonic acid 6-(4-allyl-piperazin-1-yl)-pyridin-3-yl ester

10 A flask containing 45 mg of palladium(II) acetate (0.2 mmol), 126 mg of BINAP (0.20 mmol) and 0.233 mg of sodium tert-butylate in dry toluene (15 mL) was flushed with nitrogen 1.275 g of 1-allylpiperazin (10 mmol) were added and the reaction mixture was heated to 50 °C. 630 mg of 4-isopropyl-benzenesulfonic acid 6-chloro-pyridin-3-yl ester (2.0 mmol) were dissolved in toluene and the solution was slowly added over a period of 10 minutes into the

15 reaction mixture with stirring. The mixture was heated to reflux with stirring for 7 h. Thereby 4-isopropyl-benzenesulfonic acid 6-(4-allyl-piperazin-1-yl)-pyridin-3-yl ester was obtained in 21 % yield.

MS [m+1]: 402

20

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm]   7.8 (d, 2H); 7.7 (d, 1H); 7.6 (d, 2H); 7.2 (dd, 1H); 6.8 (d, 1H); 5.8 (m, 1H); 5.2 (m, 2H); 3.5 (m, 4H); 3.0 (m, 3H); 2.5 (m, 4H); 1.2 (d, 6H).

Example 60: 4-Isopropyl-benzenesulfonic acid 6-(4-propyl-piperazin-1-yl)-pyridin-3-yl ester,
25 hydrochloride

In a reaction flask 5 mg of palladium on charcoal were added to 50 mg of 4-isopropylbenzenesulfonic acid 6-(4-allyl-piperazin-1-yl)-pyridin-3-yl ester from example 59(0.12 mmol) in dry ethyl acetate (5 ml). The atmosphere was then charged with hydrogen

30 gas and the reaction mixture was stirred at room temperature for 1 hour. Thereby, 4-isopropyl-benzenesulfonic acid 6-(4-propyl-piperazin-1-yl)-pyridin-3-yl ester were obtained in 58 % yield. The compound was converted into its hydrochloride salt by addition of HCl in ether.

35 MS [m+1]: 404

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm]   11.0 (bs, 1H); 7.8 (m, 3 H); 7.6 (d, 2 H); 7.3 (dd, 1H); 6.9 (d, 1H); 4.3 (d, 2H); 3.5 (d, 2H); 3.3 (dd, 2H); 3.0 (m, 5H); 1.7 (m, 2H); 1.3 (d, 6H); 0.9 (t, 3H).

40

Examples of galenic administration forms

A)   Tablets

5   Tablets of the following composition are pressed on a tablet press in the customary manner:

   40 mg of substance from Example 2
   120 mg of corn starch
   13.5 mg of gelatin
10   45 mg   of lactose

   2.25 mg of Aerosil® (chemically pure silicic acid in submicroscopically fine dispersion)
   6.75 mg of potato starch (as a 6% paste)

B)   Sugar-coated tablets

15

   20 mg of substance from Example 2
   60 mg of core composition
   70 mg of saccharification composition

20   The core composition consists of 9 parts of corn starch, 3 parts of lactose and 1 part of 60:40 vinylpyrrolidone/vinyl acetate copolymer. The saccharification composition consists of 5 parts of cane sugar, 2 parts of corn starch, 2 parts of calcium carbonate and 1 part of talc. The sugar-coated tablets which had been prepared in this way are subsequently provided with a gastric juice-resistant coating.

25

Biological investigations – receptor binding studies:

The substance to be tested was either dissolved in methanol/Chremophor® (BASF-AG) or in dimethyl sulfoxide and then diluted with water to the desired concentration.

30

Dopamine D_3 receptor:

The assay mixture (0.250 ml) was composed of membranes derived from ~ 10^6 HEK-293 cells possessing stably expressed human dopamine D_3 receptors, 0.1 nM [^{125}I]-iodosulpride

35   and incubation buffer (total binding) or, in addition, test substance (inhibition curve) or 1μM spiperone (nonspecific binding). Each assay mixture was run in triplicate.

The incubation buffer contained 50 mM tris, 120 mM NaCl, 5 mM KCl, 2 mM $CaCl_2$, 2 mM $MgCl_2$ and 0.1% bovine serum albumin, 10 μM quinolone and 0.1% ascorbic acid (prepared

40   fresh daily). The buffer was adjusted to pH 7.4 with HCl.

70

Dopamine D_{2L} receptor:

The assay mixture (1 ml) was composed of membranes from ~ 10^6 HEK-293 cells possess-
5   ing stably expressed human dopamine D_{2L} receptors (long isoform) and 0.01 nM [^{125}I] iodos-
piperone and incubation buffer (total binding) or, in addition, test substance (inhibition curve)
or 1µM haloperidol (nonspecific binding). Each assay mixture was run in triplicate.

The incubation buffer contained 50 mM tris, 120 mM NaCl, 5 mM KCl, 2 mM $CaCl_2$, 2 mM
10    $MgCl_2$ and 0.1% bovine serum albumin. The buffer was adjusted to pH 7.4 with HCl.

Measurement and analysis:

After having been incubated at 25°C for 60 minutes, the assay mixtures were filtered through
15   a Whatman GF/B glass fiber filter under vacuum using a cell collecting device. The filters
were transferred to scintillation viols using a filter transfer system. After 4 ml of Ultima Gold®
(Packard) have been added, the samples were shaken for one hour and the radioactivity
was then counted in a Beta-Counter (Packard, Tricarb 2000 or 2200CA). The cpm values
were converted into dpm using a standard quench series and the program belonging to the
20   instrument.

The inhibition curves were analyzed by means of iterative nonlinear regression analysis us-
ing the Statistical Analysis System (SAS) which is similar to the "LIGAND" program de-
scribed by Munson and Rodbard.
25

In these tests, the compounds according to the invention exhibit very good affinities for the
D_3 receptor (< 100 nM, frequently < 50 nM) and bind selectively to the D_3 receptor.
The results of the binding tests are given in Table 1.

30   Table 1:

Example	K_i (D_3) [nM]	Selectivity vs. D_2L*
1	3.0	232
2	5.5	25
3	5.9	15
5	11.4	108
6	9.7	169
7	11.4	68
10	7.5	93
11	6.2	77
13	3.6	131
13a	2.7	96

Example	K_i (D$_3$) [nM]	Selectivity vs. D$_2$L[*]
14	2.5	81
14a	1.5	184
16	3.8	131
17	8.2	148
19	36.9	91
22	21.9	22
24	25.0	47
27	21.4	55
28	25.3	67
29	16.9	31
30	11.1	17
31	14.0	96
32	17.0	74
34	9.6	73
35	26.6	51
36	5.4	50
37	2.7	86
38	17.2	22
39	34.6	30
42	5.3	33
43	1.1	80
44	1.4	41
45	1.4	24
46	7.1	50
47	6.1	118
48	0.8	21
49	0.4	19
50	9.9	57
51	3.1	101
52	14.2	63
53	8.8	149
54	2.3	84
55	2.9	159
56	1.6	399
57	7.3	234
58	6.2	254
59	16.2	75
60	17.4	47

[*] $K_i(D_3)/K_i(D_{2L})$